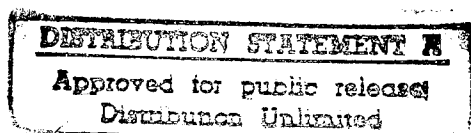


*Department  
of  
Clinical Investigation  
Annual Research Progress Report*

19960212 258



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**Fiscal Year 1995**  
**Madigan Army Medical Center**  
**Tacoma, Washington**

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Nancy Whitten

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Madigan Army Medical Center  
Tacoma, WA 98431-5000

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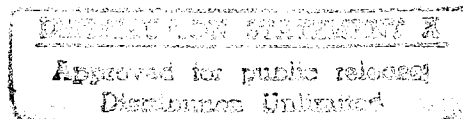
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This report covers all research protocols that were administratively or technically supported by the Department of Clinical Investigation, Madigan Army Medical Center, during FY 95. Included in the individual reports are title, investigators, funding, objective, technical approach, and progress for FY 95. Also included in the report are rosters for the Department, funding information, and presentations and publications emanating from Madigan Army Medical Center during FY 95.

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**ANNUAL PROGRESS REPORT**

**30 SEPTEMBER 1995**

**DEPARTMENT OF CLINICAL INVESTIGATION  
MADIGAN ARMY MEDICAL CENTER  
TACOMA, WASHINGTON 98431-5000**

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# **ANNUAL RESEARCH PROGRESS REPORT**

**FISCAL YEAR 1995**

**DEPARTMENT OF CLINICAL INVESTIGATION  
MADIGAN ARMY MEDICAL CENTER  
TACOMA, WASHINGTON 98431**

## **INTRODUCTION**

In conducting the research described in this report, the investigators adhered to the "Guide for the Care and Use of Laboratory Animals" as prepared by the Committee on the Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources, National Institutes of Health, and Title 9, Subchapter A, Parts I, II, and III of the Code of Federal Regulations. The investigators adhered to Title 21, Part 50 of the Code of Federal Regulations and the recommendations from the Declaration of Helsinki in the performance of investigations involving human subjects.

## **ACKNOWLEDGEMENTS**

I would like to take this opportunity to thank MAJ Curtis Yeager, Nancy Whitten, Barbara Jones, and Troy Patience for the effort which is obvious in the compilation, preparation, and editing of this publication.

## FOREWORD

In FY 95 the number of new protocols submitted and total protocols managed again reached a new high. During this FY, DCI processed 190 new protocols and managed 504 total protocols during the year. MAMC investigators continued to attract clinical trials at an increasing rate, augmenting their extramural funding through multiple foundations. MAMC nurses were again successful in competing for Tri-service Nursing research funding, bringing in over \$250,000 in DOD nursing research funding. The department continued its strong thrust in molecular biology, training 12 fellows and staff in hands-on techniques and making progress in the areas of characterizing wild-type and alternate SHBG mRNA transcripts in breast cancer (Dr. Kathy Moore), exquisitely sensitive detection of bacteria by PCR in amniotic fluid of pre-term deliveries (CPT Keith Martin), evaluating the presence of telomerase activity in multiple cancers (CPT Wade Aldous) and detection of bcl-2, bak and p53 gene products in therapeutically induced apoptosis in breast cancer cell lines (MAJ Rich Williams). As assistant chief and Director of Surgical Research, LTC Rich Sherman has energized research productivity in the Department of Surgery, and especially the Orthopedic service. MAJ Curtis Yeager also joined the department as C, Immunology and director of the newly created Research Support Service. MAJ Ron Nielsen filled the veterinary void left by the departure of CPT Steve Caldwell mid-year and has begun to build up the animal research capability of the department. The support of MG James Peake, Commander, COLs Al Buck and Darrell Porr, DCCS, COL Thad Krupka, DCA and COL Charles Mitchell, Director of Medical Education is gratefully acknowledged for its role in the department fulfilling its mission.

## UNIT SUMMARY

### 1. Objective

To provide the facilities and environment to stimulate an interest in clinical and basic investigations within Madigan Army Medical Center.

### 2. Technical Approach

<u>Description</u>	<u>MANPOWER</u>	
	<u>Rank</u>	<u>MOS</u>
Chief, Clinical Investigation MOORE, Dan C., M.D., COL, MC	O6	60P9A
Chief, Clinical Studies Service VACANT		
Director, Surgical Research Service SHERMAN, Richard A., Ph.D., LTC, MS (EOD Oct 94)	O5	71F67
Chief, Lab Animal & Surgery Service CALDWELL, Stephen, D.V.M., CPT, VC (ETS Nov 94)	O3	64A00
Chief, Lab Animal & Surgery Service NEILSEN, Ronald E., D.V.M., MAJ, VC (EOD Aug 95)	O4	64C00
Chief, Immunology Service YEAGER, Curtis L., Ph.D., MAJ, MS (EOD Aug 95)	O4	71A67
Chief, Bioresearch Service MARTIN, Rodger K., Ph.D., CPT(P), MS	O3	71B9C
Chief, Microbiology Service ALDOUS, Wade K., Ph.D., CPT, MS (EOD Oct 94)	O3	71A67
NCOIC HERNANDEZ, Carlos I., SFC	E7	91K4R
Senior Animal Care Sgt. BARRETT, Vickie R., SFC (EOD Dec 94)	E7	91T4R
Senior Animal Care Sgt. BROWN, Bruce A., SGT	E5	91T2R
Animal Care Specialist DELUCIA, Julie A., SGT	E5	91T10
Lab Tech KEENE, Corey A., SPC (EOD Jul 95)	E4	91K10
Lab Tech WIEGAND, Neil, SPC (ETS May 95)	E4	91K10

Manpower (continued)

<u>Description</u>	<u>Rank</u>	<u>MOS</u>
Lab Tech POOL, Rosemary, PFC	E4	91K1R
Lab Tech BOUMA, Cheri Ann, PFC (EOD Jul 95)	E3	91K10
Research Admin Scientist MOORE, Katherine H., Ph.D.	GS13	0601
Med Tech MATEJ, Louis A., B.S., M.T.	GS11	0644
Med Tech WRIGHT, James R., B.A., M.T.	GS11	0644
Med Tech STYNER, M. J., B.S., M.T.	GS11	0644
Med Tech THOMSON-ARCHER, Kelly, B.S., M.T.	GS11	0644
Med Tech BULLOCK, Jeff M., B.S., M.S., M.T. (EOD Jan 95)	GS09	0644
Statistician Medical PATIENCE, Troy H., B.S.	GS09	1530
Edit Asst/Steno WHITTEN, Nancy J., B.A.	GS09	1087
Sec/Steno HOUGH, Eugenia R.	GS06	0318
Maintenance Worker KAEO, Curtis	WG7	4749
Med Tech CRISS-TILLOTSON, Mary "Tilly"* (Dec 92 - Dec 95)	GS09	0644

\* Breast Cancer Program Employee

### **Funding FY 95**

Civilian Salaries	\$398,100
Military Salaries	411,200
Consumable Supplies	103,000
Contractual Services	1,300
BLIC "C" MEDCASE Equipment	647,080
Capital Equipment	189,791
TDY - departmental	6,600
TDY - departmental presentations	5,415
TDY - Research presentations	37,953
	\$1,800,439

### **EXTRAMURAL FUNDING:**

Federal sources:	
Tri-service Nursing	\$989,764
USAMRDC	\$536,127
Non-federal sources:	
FACT	\$143,333
PC3	\$102,540
HMJ	\$1,254,604
TOTAL EXTRAMURAL FUNDING:	\$3,026,368

<b>GRAND TOTAL</b>	<b>\$4,826,807</b>
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### 3. Progress

During FY 95, there were 504 active protocols that received administrative and/or technical support during the year. Of these, 352 are presently ongoing; 3 are in a suspended status, 103 were completed; and 46 were terminated. The principal investigator distribution was as follows: 385 staff protocols (includes 186 group oncology protocols); 61 resident protocols, 43 fellow protocols, 4 intern protocols, and 9 active duty student protocols. There were 190 new protocols.

There were 90 publications in nationally recognized journals and 111 presentations at regional or national medical association meetings.

### 4. Fellowship/Residency Program Support

Fellowship/Residency programs supported by DCI: 23  
126 protocols involving 110 residents  
137 protocols involving 25 fellows

### 5. Other training programs supported by DCI:

Training protocols: (1) Department of Surgery: 3  
(2) Department of Emergency Medicine: 2  
(3) Department of Pediatrics: 1  
(4) Department of OB/GYN: 1  
(5) Department of Clinical Investigation: 1  
(6) Department of Medicine: 1  
(7) I Corps: 2

### 6. Other protocols supported:

1 USDA protocol  
1 USN protocol

## COMMITTEE MEMBERS

Commander  
Madigan Army Medical Center  
MG JAMES B. PEAKE, M.D., MC

### Clinical Investigation Committee

Chairman  
Chief, Clinical Investigation  
COL Dan C. Moore, M.D., MC

Chief or delegated representative of:

Department of Pediatrics  
Department of OB/GYN  
Department of Family Practice  
Department of Emergency Medicine  
Department of Nursing  
Department of Medicine  
Department of Surgery  
Department of Pathology  
Department of Radiology  
Pharmacy Service  
Surgical Research Service, DCI  
Clinical Studies Service, DCI  
Microbiology Service, DCI  
Biochemistry Service, DCI  
Bioresearch Service, DCI  
Immunology Service, DCI  
Lab Animal and Surgery Service, DCI  
Medical Statistician, DCI

## COMMITTEE MEMBERS (CONT'D)

### Human Use Committee

Chairman  
Chief, Clinical Investigation  
COL Dan C. Moore, M.D., MC

Chief or delegated representative of:

Department of Nursing  
Department of Radiology  
Department of Ministry and Pastoral Care  
Pharmacy Service  
Social Work Service  
Center Judge Advocate  
Non-institutional member  
Surgical Research Service, DCI

## COMMITTEE MEMBERS (CONT'D)

### Animal Use Committee

Chairman

Chief, Surgical Research Service, DCI  
LTC Richard Sherman, MS

Chief or delegated representative of:

Department of Clinical Investigation  
Lab Animal & Surgery Service  
Department of Nursing  
Veterinary Services  
Non-institutional member  
Chief, NW Veterinary Service Support Area  
NCOIC, Lab Animal & Surgery Service, DCI

## BRYON L. STEGER RESEARCH AWARD

This award is given to residents, submissions are judged on their scientific merit, relevance, objectivity of evaluation, interpretation of results, and the potential importance of the subject of the research.

Recipient of this award for 1995: CPT Jamie Kendrick Waselenko, MC, Resident, Internal Medicine, for her research protocol:

*Prolonged Room Temperature Storage of Thyroid Crude Cell Lysate with Subsequent Recovery of DNA*

Other nominees were:

*Adolescent Risk Behavior and the Influence of Parents and Education* by MAJ Brent V. Nelson, MC

*The Impact of Multiple Neuroimaging Studies on Classification, Treatment, and Outcome I Acute Ischemic Stroke* by CPT Stephen M. Salerno, MC

*The Normal Flora of the Human Epididymis* by CPT Bradley F. Schwartz, MC

*Factors Associated with Marital Satisfaction Among Physicians and Their Spouses* by CPT Kevin deWeber, MC

## FELLOW'S RESEARCH AWARD

This award is given to fellows, submissions are judged on their scientific merit, relevance, objectivity of evaluation, interpretation of results, and the potential importance of the subject of the research.

Recipient of this award for 1995:

CPT Lloyd Hancock, MC, Department of Medicine, Endocrinology Service for his research protocol entitled *The Effect of Propylthiouracil on Subsequent Radioactive Iodine Therapy in Graves' Disease*.

Other nominees were:

LTC Donald M. Bradshaw, Department of Family Practice for his research protocol entitled *A Survey of The Non-Clinical Roles of Army Family Physicians in Thier Initial Post-Residency Assignment and Their Level of Preparedness for These Roles*.

CPT Scott Sample, Department of Medicine, Cardiology Service for his research protocol entitled *Influence of Smoking, Nicotine Replacement Therapy and Smokeless Tobacco on Hemostatic Function in Healthy Men and Women*.

CPT Lisa Zacher, Department of Medicine, Pulmonary Service for her research protocol entitled *Prospective Comparison of Computed Tomography and Fiberoptic Bronchoscopy in Patients with Unexplained Hemoptysis and Non-suspicious Chest Radiographs*.

MAJ Michael Rave, Department of Medicine, Cardiology Service for his research protocol entitled *Morphologic Variables Associated with Adverse Outcome During Right Coronary Artery Balloon Angioplasty*.

## PRESENTATIONS

### FISCAL YEAR 95

#### DEPARTMENT OF CLINICAL INVESTIGATION

Martin RK, Markenson GR, Bullock J, Foley K	The Detection of Atrial Natriuretic Factor mRNA from Placentas in Normal and Preeclamptic Pregnancies.	Conference on Military Perinatal Research, Aspen, USA, September 95.
Martin RK, Markenson GR, Tillotson-Criss M, Foley K, Yancey MK	The Relationship of Bacterial Contamination and Interleukin-6 in Amniotic Fluid in Preterm Labor and Delivery.	Conference on Military Perinatal Research, Aspen, USA, September 95.
Moore KH, Bertram KA, Gomez RR, Styner MJ, Matej LA	Is Sex Hormone Binding Globulin Locally Produced in Breast Cancer Tissue?.	Endocrine Society, October 94.
Moore KH, Styner MJ, Matej LA, Plymate SR	Alternate Sex Hormone Binding Globulin (SHBG) mRNA Transcripts Produced by Prostate Cells.	Society for the Study of Reproduction, Davis, USA, 1995
Sherman RA, Goeken AFW, Blanchard E, Andrasik F, Arena J, DeGood D, Glaros A, Wolf S	Five Month Progress Report for the NIH Supported Study Entitled: Biofeedback for Pain: A Multipractitioner Outcome.	Association for Applied Psychophysiology and Biofeedback, 26th Annual Meeting, Cincinnati, USA, March 95.

#### DEPARTMENT OF DENTISTRY

Vorona AA	Delayed Primary Closure of Maxillofacial Wounds.	American Association of Oral and Maxillofacial Surgeons Clinical Congress, Orlando, USA, February 95.
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#### DEPARTMENT OF EMERGENCY MEDICINE

Frohna WJ	Effectively Communicating With Consultants.	Joint Services Symposium, Emergency Medicine on the Riverwalk, San Antonio, USE, January 95.
Frohna WJ	Teaching and Evaluating Interpersonal Skills in the Emergency Department.	Society for Academic Emergency Medicine, San Antonio, USE, May 95.
Frohna WJ	Effectively Communicating With Consultants.	American College of Emergency Physicians Scientific Assembly, Washington DC, USA, October 95.
Nold JM, Handley JK, Vanderlinde JJ, Pace SA, Guertler AT	Corneal Abrasions: Is Eye Patching Necessary?.	Triservice Course in Emergency Medicine, San Diego, USA, January 95.

## PRESENTATIONS - MAMC - FY 95

Vaccaro AR, Rudman NT	Blood Cultures in Urinary Tract Infections Requiring Hospitalization: Necessity of Habit?	Tri-Service Course in Emergency Medicine, San Diego, USA, January 95.
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## DEPARTMENT OF FAMILY PRACTICE

Boam WD, Miser WF	Is Ultrasound Reliable for Diagnosing Stress Fractures?	20th Annual Uniformed Services Academy of Family Physicians, San Diego, USA, April 95.
DeWeber K	Factors Associated With Physicians's Marriage Satisfaction.	USAFP, San Diego, USA, April 95.
Dombrowski RT	Comparison of Partner-Resistant Exercise Programs (Eccentric and Concentric) versus Calisthenics for Upper Body Conditioning.	USAFP Annual Scientific Assembly, San Diego, USA, April 95.
Gloriosos JE, Miser WF	Potential for Secondary Near Drowning After Salt Water Immersion.	20th Annual Uniformed Services Academy of Family Physicians, San Diego, USA, April 95.
Miser WF	The Practice of Obstetrics by Army Family Physicians.	American Academy of Family Physicians Scientific Assembly, Anaheim, USA, September 95.
Miser WF	The Correlation of Personal Health Risk Appraisals and Attitudes Toward Health Promotion in Military Family Physicians.	7th Annual Health Promotion Conference, Herndon, USA, August 95.

## DEPARTMENT OF MEDICINE, ENDOCRINOLOGY SERVICE

Bunner DL, Williams T, Tuttle RM	Physiologic Correlates of Body Mass Index in NIDDM: Do Lean NIDDM Patients Have Lower Cardiovascular Risk?	American Society for Clinical Pharmacology and Therapeutics, San Diego, CA, March 95.
Lesho E, Jones RE	Hypothyroid Graves' Disease-An Immunologic Chameleon.	American College of Physicians, Reston, USA, September 95.
Reed HL, LeMar HJ, Jones RE, Bunner DL, Lance J, Moon M, Gibson CA	Submaximal Cycloergometry to Evaluate Recovery From Hypothyroxinemia Following 131I Therapy for Thyrotoxicosis.	Endocrine Society, Washington DC, USA, June 95.

## DEPARTMENT OF MEDICINE, HEMATOLOGY/ONCOLOGY SERVICE

Caton J, Ellis RB	Male Breast Cancer: The Department of Defense Experience.	American Society of Clinical Oncology, Los Angeles, CA, May 95.
Caton J, Ellis RB	Male Breast Cancer: The Department of Defense Experience.	11th Annual Army Regional Meeting of the American College of Physicians, Reston, USA, October 94.

## DEPARTMENT OF MEDICINE, INTERNAL MEDICINE SERVICE

Landry FJ	Drug Usage Study of Felodipine.	Society of General Internal Medicine, San Diego, USA, May 95.
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Salerno SM, Landry  
FJ, Schnick JD,  
Schoomaker EB

Do Multiple Neuroimaging Studies Affect  
Treatment and Patient Outcomes.

PRESENTATIONS - MAMC - FY 95

American College of Physicians  
National Meeting, Atlanta, USA,  
March 95.

DEPARTMENT OF MEDICINE, NEUROLOGY SERVICE

Dawson WJ, Charness  
M, Goode DJ,  
Lederman RJ, Leek JC,  
Newmark J

Terminology in Performing Arts Medicine.

13th Annual Cleveland Clinic  
Symposium on Performing Arts  
Medicine, Aspen, USA, July 95.

Hassid EI, Elliott MA

A Case of Language Dysfunction Associated  
With Cerebellar Infarction.

14th Annual AMEDD  
Conference, Bethesda, USA,  
November 94.

Kesting L

Abulic State Associated With Caudate  
Stroke.

14th Annual AMEDD  
Conference, Bethesda, MD,  
November 94.

Marden LA

A Case of Recurrent Hemorrhagic  
Leukoencephalitis With Neuropathology and  
MRI Correlation.

14th Annual AMEDD Neurology  
Conference, Bethesda, USA,  
November 94.

Marden LA, Rosenberg  
MI, May EF

The Significance of Unilateral Rebound,  
Nystagmus and Conjugate Eye.

The Association for Research in  
Vision and Ophthalmology, Ft  
Lauderdale, FL, May 95.

Newmark J, Weinstein  
MS

A Proposed Standard Music-Medicine  
Examination.

Performing Arts Medicine  
Association Annual Meeting,  
Aspen, USA, July 95.

DEPARTMENT OF MEDICINE, PULMONARY SERVICE

Dillard TA, Knutsen  
SW, Phillips YY, Berg  
BW, Mehm WJ,  
Criswell D

Prevention of Altitude Hypoxemia:  
Comparison of an Oxygen Conserving  
Device with Nasal Cannulae.

American Thoracic Society,  
Poster Discussion Session,  
Seattle, USA, May 95.

Lawless NP, Dillard  
TA, Davis Q,  
Kamimori G

Effects of carbohydrate ingestion on  
hypoxemia at 15,000 feet of simulated  
altitude in normal subjects.

American Thoracic Society,  
Poster Discussion Session,  
Seattle, USA, May 95.

Murray TR,  
O'Loughlin J,  
Thompson JW, Roth  
BJ

Physiologic Effect of Therapeutic Lung  
Radiation on Exercise.

American Thoracic Society,  
Poster Discussion Session,  
Seattle, USA, May 95.

Parker JM, Dillard TA,  
Phillips YY

Arm Span to Height Relationships in  
Patients Referred for Spirometry.

American Thoracic Society,  
Thematic Poster Session, Seattle,  
USA, May 95.

Roth BJ, Meyer CA

Computed Tomographic Evidence of  
Coronary Calcification as a Predictor for  
Cardiac Complications of Thoracic Surgery.

American Thoracic Society,  
Poster Discussion Session,  
Seattle, USA, May 95.

Weber PV

ALS/PD Complex of Guam.

14th Annual AMEDD  
Conference, Bethesda, USA,  
November 94.

Winter MG, Pike JD,  
Dillard TA

Measurement of Weaning Parameters by  
Microprocessors versus Traditional Means.

American Thoracic Society  
Meeting, Seattle, WA, May 95.

# PRESENTATIONS - MAMC - FY 95

Zacher LL, Walsh DW, Smith DV, Cragun WH  
Comparison of a Picture Archiving and Communication System Planimetry Measurement of Total Lung Capacity with Body Plethysmography.

American Thoracic Society, Thematic Poster Session, Seattle, USA, May 95.

## DEPARTMENT OF NURSING

Chambers S	Neonatal Outcomes in a Modified NICU Environment.	Celebrating Nursing Research and Scholarship, Pacific Luthern University, Tacoma, USA, November 94.
DePaul D	Neonatal Outcomes in a Modified NICU Environment.	The Physical and Developmental Environment of the High-Risk Infant, Orlando, USA, January 95.
DePaul D, Chambers S, Zaichkin J, Imbruglio L	Fatigue Following Childbirth: Military Family Outcomes.	NANN International Clinical and Research Symposium, Tacoma/Seattle, USA, April 95.
Gilcreast D, Stotts N, Froelicher E, Lee K, Baker L, Moss K	Preliminary Findings of the Effect of Electrical Stimulation on Diabetic Foot Perfusion.	15th Annual Meeting of the Wound Healing Society, Minneapolis, USA, April 95.
Gilcreast D, Stotts N, Froelicher E, Lee K, Baker L, Moss K	Innovation and Collaboration: Responses to Health Care Needs.	Western Institute of Nursing, San Diego, USA, May 95.
Gilcreast D, Stotts N, Froelicher E, Lee K, Baker L, Moss K	Preliminary Findings of the Effect of Electrical Stimulation on Diabetic Foot Perfusion.	Graduate Research Day, University of California, San Francisco, USA, May 95.
Gilcreast D, Stotts N, Froelicher E, Lee K, Baker L, Moss K	Preliminary Findings of the Effect of Electrical Stimulation on Diabetic Foot Perfusion.	UCSF School of Nursing "Celebration of Excellence", San Francisco, USA, April 95.
Havens PJ	Critical Incident Stress Debriefing.	3rd Annual Convention of Academy of Medical/Surgical Nurses, Washington, DC, November 94.
Hill PA	Outpatient Anticoagulant Therapy Practical Aspects of Management.	10th Annual Education Conference, Uniformed Nurse Practitioner Association, Bethesda, USA, November 94.
Leander DJ, Loan LA	Exogenous Surfactant Therapy in Premature Infants.	Sigma Theta Tau Nursing Conference, Pacific Lutheran University, Tacoma, USA, February 95.
Leander DJ, Loan LA	Exogenous Surfactant Therapy in Premature Infants.	National Association of Neonatal Nurses, International Research, April 95.
Leander DJ, Loan LA	Exogenous Surfactant Therapy in Premature Infants.	Brooke Army Medical Center Nursing Research Day, San Antonio, USA, May 95.

## PRESENTATIONS - MAMC - FY 95

Mygrant BI	Postoperative Wound Healing, Hydration & Oxygenation.	Sigma Theta Tau International Conference, Pacific Lutheran University, Tacoma, USA, February 95.
Renaud MT	Neonatal Outcomes in a Modified NICU Environment.	National Association of Neonatal Nurses Annual Conference, San Antonio, USA, September 95.
Renaud MT	Neonatal Outcomes in a Modified NICU Environment.	Serving Vulnerable Populations: Issues, Programs & Policies, Seattle University, Seattle, USA, April 95.
Renaud MT	Neonatal Outcomes in a Modified NICU Environment.	NANN International Clinical and Research Symposium, Seattle, USA, April 95.
Zimbelman EE	Female Genital Mutilation.	Madigan Army Medical Center OB/GYN Clinic Nurses Lecture, Ft. Lewis, USA, March 95.
Zimbelman EE	Women & AIDS: Violence Against Women.	Madigan Army Medical Center OB/GYN Clinic Nurses Lecture, Ft. Lewis, USA, May 95.

## DEPARTMENT OF OBSTETRICS/GYNECOLOGY

Armstrong AY, Weiss TE, Hoeldtke N, Chapin BL, Tuttle RM	Fasting Insulin As a Predicator of the Response to Clomiphene Citrate in Obese Anovulatory Women.	Armed Forces District Meeting, American College of OG/GYN, Reno, NV, November 94.
Boley T, Markenson AS, Maslow AS, Kopelman JN, Read J	Does Nicotine Affect Levels of Thromboxane and Prostacyclin in the Dually Perfused Human Placental Cotyledon Model?.	Society of Perinatal Obstetricians, Atlanta, GA, January 95.
Brown ZA, Ashley R, Selke S, Zeh J, Kopelman J, Maslow A, Watts HD, Mohan K	The Frequency of HSV Seroconversion During Pregnancy and Its Impact on Pregnancy Outcome.	2nd Annual Meeting of the Infectious Disease Society for Obstetrics & Gynecology, Traverse City, USA, August 95.
Bullis WJ, Engel CC, Armstrong AY, Engel AL	Prevalence of Sexual Victimization Among Women with Chronic Pelvic Pain: A Preliminary Report.	Armed Forces District Meeting, American College of OB/GYN, Reno, NV, November 94.
Macedonia CR	Telepresence in Military Medicine.	AUSA Conference on Telepresence in Military Medicine, McLean, USA, March 95.
Markenson GR, Foley KS, Maslow AS, Kopelman JN	The Effect of Atrial Natriuretic Factor and Angiotensin II on Placental Perfusion Pressure in the Ex-Vivo Cotyledon Model.	Society of Perinatal Obstetricians, Atlanta, USA, January 95.
Maslow AS, Boley TJ, Marken GR, Kopelman JN	Does Nicotine Affect Levels of Thromboxane and Prostacyclin in the Dually Perfused Human Placental Cotyledon Model?.	Society of Perinatal Obstetricians, Atlanta, GA, January 95.

## PRESENTATIONS - MAMC - FY 95

Napolitano PG	<p> TuboOvarian Abscess After Routine Delivery. </p>	<p> AFD-ACOG 33rd Annual Meeting, Ft. Irwin, USA, November 94. </p>
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## PREVENTIVE MEDICINE SERVICE

Hack DC, Krauss MR	<p> Occupational Medicine Training: Can It Reduce Time Loss. </p>	<p> Prevention 95, American College of Preventive Medicine, New Orleans, USA, March 95. </p>
Klamerus SD, Krauss MR	<p> Vaccine Usage in Soldiers at Fort Lewis, WA: Enumeration of Unnecessary Vaccinations. </p>	<p> Prevention 95, American Coll of Preventive Medicine, New Orleans, USA, March 95. </p>

## DEPARTMENT OF PEDIATRICS

Carter ER, Behrens M, Moffitt D	<p> Are Nose Clips Necessary in Children Performing Spirometry?. </p>	<p> American Thoracic Society, International Conference, Seattle, USA, May 95. </p>
Carter ER, Webb C, Moffitt D	<p> Evaluation of A Helium-Oxygen Mixture in the Treatment of Children Hospitalized with Acute, Severe Asthma. </p>	<p> American Thoracic Society, International Meeting, Seattle, USA, May 95. </p>
Fairchok MP	<p> Age Dependent Responses to Mycobacterial Antigens. </p>	<p> USPS Military Pediatric Meeting, San Francisco, USA, March 95. </p>
Fairchok MP	<p> Penicillin Resistant Pneumococci in a Military Population. </p>	<p> USPS Military Pediatric Meeting, San Francisco, USA, March 95. </p>
Stafford EM, Stewart RS, Teague G, Gomez R, Crothers B, Michel TJ, Patience TH, Moore DC	<p> Detection of Human Papillomavirus in Cervical Biopsies of Summer Camp ROTC Cadets with Abnormal Papanicolaou Smears. </p>	<p> Uniformed Services Pediatric Seminar, 1995. </p>
Stephan MJ, Dietz J, Carpenter C, Polamar D, Byers P	<p> Progressive Kyphoscoliosis in Ehlers-Danlos Syndrome Type VI. </p>	<p> Pacific Northwest Genetics Meeting, Vancouver, Canada, December 94. </p>
Stephan MJ, Kelley RI, Anderson AJ, Walker WO	<p> Variant Smith-Lemli-Opitz Syndrome With Features of Noonan Syndrome and Atypical Sterol Metabolism. </p>	<p> David W Smith Workshop on Morphogenesis &amp; Malformations, Bozeman, USA, July 95. </p>

## DEPARTMENT OF RADIOLOGY

Crocker JD, Bender GN	<p> Antral Nodularity, Fold Thickening, and Narrowing: Upper GI Series Findings That May Indicate Chronic Gastritis Secondary to Helicobacter Pylori. </p>	<p> Annual Meeting of the Radiological Society of North America, Chicago, IL, November 94. </p>
Ho VB, Kinney JB, Sahn DJ	<p> Ruptured Sinus of Valsalva Aneurysm: Cine MR. </p>	<p> Society of Magnetic Resonance, Cardiovascular MRI Workshop, Santa Fe, USA, October 94. </p>
Mansfield LT	<p> Cost Effectiveness of Screening MRIs of the Knee Prior to all Knee Arthroscopies. </p>	<p> AMEDD Radiology Research Symposium, April 95. </p>

Meyer CA, Colvin K, Leckie R, Chakraborty D, Carter J, Cragun WH, Smith DV	Pulmonary Nodule Detection Using A Free Response ROC Analysis: Conventional Film vs. Digital vs. AMBER-Digital Radiography.	Society of Thoracic Radiology, Amelia Island, USA, March 95.
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## DEPARTMENT OF SURGERY, ANESTHESIA SERVICE

Pylman ML, Teiken PJ, Helman JD	Pressure Within the Epidural Space in Parturients and Flow in Epidural Catheters.	Western Anesthesia Resident Conference 1995, Los Angeles, USA, April 95.
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## DEPARTMENT OF SURGERY, OTOLARYNGOLOGY (ENT) SERVICE

Chismire KJ	Vision Problems of the Older Adult; Glaucoma, Cataract, and Macular Degenerations.	Pacific Northwest Conference for Primary Care Practitioners, Seattle, USA, October 94.
Edmond CV	ENT Surgical Simulator Project, "Surgical Simulation".	National Forum: Military Telemedicine On-Line Today, March 95.
Edmond CV	ENT Surgical Simulator Project, "Virtual Reality Applications in Trauma Management".	1st Trauma Symposium, San Antonio, USA, September 95.

## DEPARTMENT OF SURGERY, OPHTHALMOLOGY SERVICE

Blanton, Schallhorn, Ng JD, Gilbert, White, Parmley VC, Mader TH	Refractive Changes During Prolonged Exposure to Altitude Following Refractive Surgery.	ARVO Annual Meeting, Ft. Lauderdale, USA, May 95.
Blanton, Schallhorn, Ng JD, Gilbert, White, Parmley VC, Mader TH	Refractive Changes During Prolonged Exposure to Altitude Following Refractive Surgery.	American Society of Cataract and Refractive Surgery, San Diego, USA, April 95.
Fannin LA	Safety and Efficacy of Laryngeal Mask - Dry Eye and the Tear Film.	The Association for Research in Vision and Ophthalmology, Ft Lauderdale, USA, May 95.
Fannin LA, Raymond WR, Polaner DM, Mader TH, Mazzoli RA	Safety and Efficacy of Laryngeal Mask Airway Anesthesia for Nasolacrimal Duct Probing and Irrigation.	The Association for Research in Vision and Ophthalmology Annual Meeting, Ft. Lauderdale, USA, May 95.
George RK	High Serum Levels of Soluble ICAM-1 (CD54) in Uveitis Patients Predict Underlying Systemic Disease.	The Association for Research in Vision and Ophthalmology Poster Presentation, Ft. Lauderdale, USA, May 95.
Gilbert, George DP, Parmley VC	Analysis of Metallic Debris Following Phacoemulsification.	The Association for Research in Vision and Ophthalmology Poster Presentation, Ft. Lauderdale, USA, May 95.
Hadley SC, Truxal AR, Krolicki TJ	Duration of Pressure Lowering Effect Utilizing Pre-Operative Intraocular Pressure Reduction Device.	The Association for Research in Vision and Ophthalmology, Ft Lauderdale, USA, May 95.

# PRESENTATIONS - MAMC - FY 95

Ng JD, White, Parmley VC, Hubickey, Carter, Mader TH	Effects of Simulated Altitude on Post Radial Keratotomy Corneas.	American Academy of Ophthalmology Meeting, San Francisco, USA, October 94.
Parmley VC, Ng JD, Rotkis, Gee, Mader TH	Penetrating Keratoplasty for Complications of Radial Keratotomy.	American Academy of Ophthalmology Meeting, San Francisco, USA, October 94.
Witkop GS	Surgical Considerations for Glaucoma Implant Surgery.	Walter Reed Ophthalmologic Research Symposium, Washington, USA, March 95.
Witkop GS	Anatomic Considerations for Ahmed Valve Placement.	The Association for Research in Vision and Ophthalmology, Annual Meeting, Ft Lauderdale, USA, May 95.
Witkop GS, George DP, Chismire KJ, Leen MM	Anatomic Considerations in Glaucoma Implant Surgery.	The Association for Research in Vision and Ophthalmology, Annual Meeting, Ft Lauderdale, USA, May 95.

## DEPARTMENT OF SURGERY, ORTHOPEDICS SERVICE

Carpenter CT	Physcal Bar Excision - A Multicenter Study.	Pediatric Orthopaedic Society of North America, Miami, FL, April 95.
Johnstone FL	Experimental Tendon Repair: Comparison of CO <sub>2</sub> Laser Welding With Ependinous Suture Technique.	25th Anniversary Meeting of the Eastern Orthopaedic Association, Southhampton, Bermuda, October 94.

## DEPARTMENT OF SURGERY, UROLOGY SERVICE

Schwartz BF	The role of cystoscopy prior to radical prostatectomy.	Northwest Urologic Society, Seattle, USA, December 94.
Schwartz BF	Small Cell Carcinoma of the Prostate.	Northwest Urologic Society, Seattle, USA, December 94.
Schwartz BF	Small Cell Carcinoma of the Prostate.	James C. Kimbrough Urological Seminar, Forty-Second Annual Meeting, Charleston, USA, January 95.
Schwartz BF	The Value of Cystoscopy Prior to Radical Prostatectomy.	Admiral Eske Research Seminar, Assoc Military Osteopathic Physicians & Surgeons, Monterey, USA, March 95.
Thrasher JB	Impotence Following TURP.	Northwest Urological Society, Forty-First Annual Meeting, Seattle, USA, December 94.
Thrasher JB	The Value of Cystoscopy Prior to Radical Prostatectomy.	Northwest Urological Society, Forty-First Annual Meeting, Seattle, USA, December 94.

PRESENTATIONS - MAMC - FY 95

Thrasher JB	Small Cell Carcinoma of the Prostate.	Northwest Urological Society, Forty-First Annual Meeting, Seattle, USA, December 94.
Thrasher JB	Radical Cystoprostatectomy for Transitional Cell Carcinoma of the Prostate.	James C. Kimbrough Urological Seminar, Forty-Second Annual Meeting, Charleston, USA, January 95.
Thrasher JB	Immunohistochemical Localization of Insulin-Like Growth Factor Binding Proteins -2 and -3 in Prostate Tissue.	James C. Kimbrough Urological Seminar, Forty-Second Annual Meeting, Charleston, USA, January 95.
Thrasher JB	Insulin-Like Growth Factor Binding Protein (IGFBP)-2 is Increased and IGFBP-3 is Decreased in vivo in Human Prostate Malignant Cells.	The Endocrine Society, Seventy-Seventh Annual Meeting, Washington, USA, June 95.
Thrasher JB	Insulin-Like Growth Factor Binding Protein-5 is Part of the Mechanism for Stromal Regulation of Prostate Epithelial and Fibroblast Cell Growth in the Human Prostate.	The Endocrine Society, Seventy-Seventh Annual Meeting, Washington, USA, June 95.
Thrasher JB	Comparative Study of Clinical Efficacy of Two Dosing Regimens of Eulexin.	Schering Oncology Speaker Update, Las Croabas, PR, September 95.
Thrasher JB, Schwartz BF	The Value of Cystoscopy Prior to Radical Prostatectomy.	James C. Kimbrough Urological Seminar, Forty-Second Annual Meeting, Charleston, USA, January 95.
Thrasher JB, Schwartz BF	Prognostic Value of Serum Beta Human Chorionic Gonadotropin Levels in Stage I Seminoma.	James C. Kimbrough Urological Seminar, Forty-Second Annual Meeting, Charleston, USA, January 95.





## PUBLICATIONS

FISCAL YEAR 95

### REGION 11 HEALTH SERVICES SUPPORT AREA

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Petty MK	Managed Care in the Military "The Madigan Army Medical Center Experience with Building a Primary Care Network". Health Care Innovations.
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### DEPARTMENT OF CLINICAL INVESTIGATION

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Levine M, Lawrence D, Moore DC, Matej LA	Acclimation of a Non-Indigenous Sub-Arctic Population: Seasonal Variation in Thyroid Function in Interior Alaska. Comp Biochem Physiol 111(2): 209-214, 1995.
Martin RK, Archer KT, Tuttle RM	Detection of PTC in Archival Formalin-Fixed, Paraffin-Embedded Tissues; Comparison of Radiolabeled DNA Hybridization and Direct Incorporation of Digoxigenin-11-dUTP Into RT-PCR Products. Diagnostic Molecular Path 3(4): 233-239, 1994.

### DEPARTMENT OF EMERGENCY MEDICINE

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Burke TF, Payne LE, Hurley WT, Bender GN, Zimba FA, Daines MC	An Unusual Case of Back Pain and Spinal Cord Compression. American J Emergency Medicine 12(6): 645-649, 1994.
Frohna WJ	Iatrogenic Magnesium Overdose in a Patient With Suspected Acute Myocardial Infarction. American J Emergency Medicine 13(4): 436-437, 1995.
Guertler AT, Pearce WA	A Prospective Evaluation of Benzocaine-Associated Methemoglobinemia in Human Beings. Annals of Emergency Medicine 24(4): 626-630, 1994.

### DEPARTMENT OF FAMILY PRACTICE

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Boam WD, Miser WF	Acute Focal Bacterial Pyelonephritis. American Family Physician 52(3): 919-924, 1995.
Lesho EP	Recognition and Management of von Hippel-Lindau Disease. American Family Physician 50(6): 1269-1272, 1994.
Miser WF, Lillegard WA, Dukas W	Injuries and illnesses incurred by an Army Ranger Unit During Operation Just Cause. Military Medicine 160(8): 373-380, 1995.

### DEPARTMENT OF MEDICINE, CARDIOLOGY SERVICE

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Eisenhauer MD, Eliasson AH, Taylor AJ	Incidence of Cardiac Arrhythmias During Intravenous Pentamidine Therapy in HIV Infected Patients. ACC Current Journal Review 4(3): 54, 1995.
Heric B, Lytle BW, Miller DP, Rosenkranz ER, Lever HM, Cosgrove DM	Surgical Management of Hypertrophic Obstructive Cardiomyopathy. J Thorac Cardiovasc Surg 110(1): 195-208, 1995.
Olson JP, Chamusco RF	Giant Left Main Coronary Artery Aneurysm Initially Seen as an Acute Coronary Syndrome. American Heart J 129(6): 1216-1217, 1995.

DEPARTMENT OF MEDICINE, CRITICAL CARE MEDICINE

Lesho EP	Can Glucose-6-Phosphate Dehydrogenase Deficiency be Correlated With ABO Blood Type?. Mil Med 159(10): 664-665, 1994.
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DEPARTMENT OF MEDICINE, DERMATOLOGY SERVICE

Crowe MA, James W	Allergic and Irritant Contact Dermatitis IN TEXTBOOK OF MILITARY MEDICINE, Military Dermatology, pgs 111-142, 1995, Published by the Office of the Surgeon General, 95.
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Kodama BF, Fitzpatrick JE, Gentry RH	Tularemia. Cutis 54(4): 279-280, 1994.
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O'Donnell BP, Mulvaney MJ, James WD, McMarlin SL	Thin Tangential Excision of Tattoos. Dermatol Surg 21(7): 601-603, 1995.
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DEPARTMENT OF MEDICINE, ENDOCRINOLOGY SERVICE

Bell BK	Gynecomastia IN McDermott MT (Ed) Endocrinology Secrets, Hanley & Belfus Medical Publishers, 231-233, 1995.
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Chapin BL, Jones RE	Infertility IN Endocrinology Secrets, 249-253, 1995.
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Gibson CA, Jones RE	Endocrine Abnormalities in Human Immunodeficiency Virus Infection. Jour US Army Med Dept 8: 14-17, 1994.
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Hibbert ML	Medical Treatment of Male Infertility IN GYNECOLOGY & OBSTETRICS, Sciarra JJ eds. 5: 1-18, 1995.
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Hibbert ML, Burry KA	Endocrinology of the Puerperium IN ENDOCRINOLOGY OF PREGNANCY: INFERTILITY AND REPRODUCTIVE MEDICINE CLINICS OF NORTH AMERICA, Diamond MP, DeCherney AH, eds. 5: 785, Oct 1994.
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Jones RE	Adrenal Insufficiency IN McDermott MT (Ed) Endocrinology Secrets, Hanley & Belfus Medical Publishers, 156-160, 1995.
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LeMar HJ, Georgitis WJ, McDermott MT	Thyroid Adaptation to Chronic Tetraglycine Hydroperiodide Water Purification Tablet Use. J Clin Endocrinol Metab 80: 220-223, 1995.
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Tuttle RM, Patience TH, Budd S	Treatment With Propylthiouracil Before Radioactive Iodine Therapy is Associated With a Higher Treatment Failure Rate Than Therapy With Radioactive Iodine Alone in Graves' Disease. Thyroid 5: 243-247, 1995.
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DEPARTMENT OF MEDICINE, HEMATOLOGY/ONCOLOGY SERVICE

Bagg MD, Wettlaufer JN, Willadsen DS, Ho VB, Lane D, Thrasher JB	Granulocytic Sarcoma Presenting as a Diffuse Renal Mass Before Hematological Manifestations of Acute Myelogenous Leukemia. Journal Urology 152(6): 2092-2093, 1994.
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Caton J, Reardon T, Ellis RB	Male Breast Cancer: The Department of Defense Experience. Proc Amer Soc Clin Oncology 14, 95.
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## DEPARTMENT OF MEDICINE, INFECTIOUS DISEASE SERVICE

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Morris JT, Beckius ML, Jeffery BS, Longfield RN, Heaven RF, Baker WJ	Lung Mass Caused by Phoma SP, In A Granulocytopenic Patient. Infect Diseases Clin Practice 4(1): 58-59, 1995.
Morris JT, Cooper RH	Intravenous Streptomycin: A Useful Route of Administration. Clin Infect Dis 19(6): 1150-1151, 1994.
Morris JT, Longfield RN	Staphylococcus Aureus Bacteremia Secondary to Postpartum Endometritis. Infections in Medicine 12(3): 129-131, 1995.

## DEPARTMENT OF MEDICINE, INTERNAL MEDICINE SERVICE

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Grathwohl K, Tenglin R, Lebrun C	Eosinophilia of the Blood, A Search For the Cause Uncovers Squamous Cell Carcinoma. Postgraduate Medicine 97(3): 169-172, 1995.
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## DEPARTMENT OF MEDICINE, NEUROLOGY SERVICE

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Dawson WJ, Charness M, Goode DJ, Lederman RJ, Leek JC, Newmark J	Terminology in Performing Arts Medicine. Journal Occupational Medicine.
Hassid EI	Neuropharmacological Therapy and Motor Recovery After Stroke. Military Medicine 160(5): 223-226, 1995.
Newmark J, Clayton WL	Persian Gulf Illnesses: Preliminary Neurological Impressions. Military Medicine 160(10): 505-507, 1995.

## DEPARTMENT OF MEDICINE, PULMONARY SERVICE

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Dillard TA, Braman S, Celli BR	COPD and Air Travel: ATS Statement, Standards for the Diagnosis and Care of Patients with Chronic Obstructive Pulmonary Disease. Am J Respir Crit Care Med 152(2): 2 Suppl, 1995.
Dillard TA, Moores LK, Bilello KL, Phillips YY	The Preflight Evaluation: A Comparison of the Hypoxia Inhalation Test With Hypobaric Exposure. Chest 107(2): 352-357, 1995.
Hnatiuk OW, Dillard TA, Torrington KG	Adherence to Established Guidelines for Preoperative Pulmonary Function Testing. Chest 107: 1294-1297, 1995.
Murray TR, O'Loughlin J, Thompson JW, Roth BJ	Physiologic Effect of Therapeutic Lung Radiation on Exercise. AJRCCM 151(4): A577, 1995.
Parker JA, Dillard TA, Phillips YY	Impact of Using Stated Versus Measured Height on Screening Spirometry. Am J Resp Crit Care Med 150(6): 1705-1708, 1994.
Roth BJ	Examining the Pleura, Editorial. Chest 107: 299-300, 1995.
Thompson JW, Grathwohl K, Ward L, Roth BJ	Videotape Education and Metered Dose Inhaler Misuse in Hospitalized Patient. Chest 108(3): 217S, 1995.

## DEPARTMENT OF NURSING

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Armstrong KK, Condron SA, McGlooin EB, McIntire SN	Cancer Prevention and Early Detection Behaviors in Military Nurses. Oncology Nursing Forum.
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- DePaul D, Chambers S      Environmental noise in the neonatal intensive care unit: Implications for nursing practice. *J Perinatal & Neonatal Nursing* 8(4): 71-76, 1995.
- Jennings BM                Nursing Research, A Time for Redirection. *J Nurs Adm* 25(4): 9-11, 1995.

#### DEPARTMENT OF OBSTETRICS/GYNECOLOGY

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- Adams MM, Sarno AP, Harlass RE, Rawlings JS, Read JA      Risk Factors for Preterm Delivery in a Healthy Cohort. *Epidemiology* 6(5): 525-532, 1995.
- Shrout AB, Kopelman JN      Ultrasonographic Diagnosis of Uterine Dehiscence During Pregnancy. *J Ultrasound Med* 14(5): 399-402, 1995.

#### PREVENTIVE MEDICINE SERVICE

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- Kirchner DB, Gaydos JC, Battigelli MC      Combustion Products of Propellants and Ammunition. *Occupational Health*: 359-396.

#### DEPARTMENT OF PATHOLOGY

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- Brissette MD, Duval-Arnould BJ, Gordon BG, Cotelingam JD      Acute Megakaryoblastic Leukemia Following Transient Myeloproliferative Disorder in a Patient Without Down Syndrome. *American Journal Hematology* 47(4): 316-319, 1994.

#### DEPARTMENT OF PEDIATRICS

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- Babonis T, Weir MR, Kelly PC, Krober MS      Progression of Tympanometry and Acoustic Reflectometry: Findings in Children With Acute Otitis Media. *Clin Pediatr* 33(10): 593-600, 1994.
- Carter ER                    Albuterol Administered by Metered-Dose Inhaler and Spacer to Young Children with Wheezing. *Arch Pediatr Adolesc Med* 148: 1352-1353, 1994.
- Carter ER                    High-Dose vs Low-Dose Systemic Corticosteroids in Acute Asthma (Letter). *Eur Respir J* 8: 1435, 1995.
- Carter ER, Moffitt D      Ibuprofen in Patients with Cystic Fibrosis (Letter). *New Engl J Med* 333: 731, 1995.
- Fairchok MP, Rouse JH, Morris SL      Age-Dependent Humoral Responses of Children to Mycobacterial Antigens. *Clin and Diag Lab Immun* 2: 443-447, 1995.
- Glenn GM, Krober MS, Kelly P, McCarty J, Weir M      Pyridoxine as Therapy in Theophylline-Induced Seizures. *Vet Human Toxicol* 37(4): 342-345, 1995.
- Kahn CA, Kelly PC, Walker WO      Lead Screening in Children With Attention Deficit Hyperactivity Disorder and Developmental Delay. *Clinical Pediatrics*: 498-501, 1995.
- Rawlings JS, Rawlings VB, Read JA      Prevalence of Low Birth Weight and Preterm Delivery in Relation to the Interval Between Pregnancies Among White and Black Women. *New England Journal Medicine* 332(2): 69-74, 1995.

#### DEPARTMENT OF RADIOLOGY

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- Do-Dai DD, Youngberg RA      MRI of the Hip With a Shoulder Surface Coil in Off-Coronal Plane. *J Computer Assisted Tomography* 19(2): 336-338, 1995.

Bender GN, Peller T, Tsuchida A, Kelley JL	Double Contrast Upper Gastrointestinal Barium Examination with Biopsy Versus Endoscopy with Biopsy in Dyspeptic Patients. Investigative Radiology 30(6): 329-333, 1995.
Crocker JD, Bender GN	Antral Nodularity, Fold Thickness, and Narrowing - Signs on the Upper GI Series That May Indicate Active Gastritis Secondary to Helicobacter Pylori. Investigative Radiology 30(8): 480-483, 1995.
Do-Dai DD, Ho VB, Rovira MJ, Knight RW, Twomey PA	Retroperitoneal Melanotic Schwannoma: Ultrasonographic Features. J Clin Ultrasound 23(1): 42-48, 1995.
Do-Dai DD, Rovira MJ, Ho VB, Gomez RR	Childhood Onset of Myxopapillary Ependymomatosis: MR Features. AJNR Am J Neuroradiol 16(4): 835-839, 1995.
Dorsay TA, Rovira MV, Ho VB, Kelley JL	Ependymoblastoma - MRI Presentation: A Case Report and Review of the Literature. Pediatric Radiology 26: 433-435, 1995.
Dorsay TA, Youngberg RA	Cine MRI of the TMJ: Need for Initial Closed Mouth Images Without the Burnett Device. J Comput Assist Tomography 19(1): 163-164, 1995.
Dorsay TA, Youngberg RA, Orr FE	Cine MRI Diagnosis and Posttherapeutic Evaluation of an Adherent TMJ Disc: A Case Report. J Oral Maxillofac Surg 52(11): 1220-1222, 1994.
Ho VB, Chuang S, Rovira M, Koo B	Juvenile Huntington Disease: CT & MR Features. AJNR 16: 1405-1412, 1995.
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Smith DV, Smith S, Bender GN, Carter JR, Kim Y, Cauthon MA, Leckie RG, Weiser JC	Evaluation of the Medical Diagnostic Imaging Support System Based on 2 Years of Clinical Experience. J Digit Imaging 8(2): 75-87, 1995.

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DEPARTMENT OF SURGERY, OTOLARYNGOLOGY SERVICE

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Place RJ, Cavanaugh DG	Computed Tomography to Diagnose Pericardial Rupture. Journal Trauma 38(5): 822-823, 1995.
Simmang CL, Rosenthal D	Tools for Laparoscopic Colectomy. Seminars in Colon & Rectal Sur 5(4): 228-238, 1994.

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Graham DA, Kinyoun JL, George DP	Endogenous Aspergillus Endophthalmitis After Lung Transplantation. Amer J Ophthalmology 119: 107-109, 1995.
Krolicki TJ, Tasman W	Cataract Extraction in Adults With Retinopathy of Prematurity. Arch Ophthalmol 113: 173-177, 1995.

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- Mader TH, Aragonés JV, Chandler AC, Hazelhurst JA, Heier J, Kingham JD, Stein E Ocular and Ocular Adnexal Injuries Treated by United States Army Ophthalmologists during Operations Desert Shield and Desert Storm. Ophthalmology Digest, 1994.
- Mader TH, White LJ Refractive Changes at Extreme Altitude After Radial Keratotomy. American J Ophthalmology 119(6): 733-737, 1995.
- Mafee MF, Ainbinder DJ, Hidayat AA Magnetic Resonance Imaging and Computed Tomography in the Evaluation of Choroidal Hemangioma. Journal of Neuroradiology 1: 67-77, 1995.
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- Ng JD, Nekola M, Parmley VC, Richardson M, Mader T Comparison of Three Corneal Trephines for Use in Therapeutic Penetrating Keratoplasties for Large Corneal Perforations. Ophthalmic Surgery 26(3): 209-215, 1995.
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#### DEPARTMENT OF SURGERY, ORTHOPEDICS SERVICE

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- Cameron SE, Wilson W, St Pierre P A Prospective, Randomized Comparison of Open vs Arthroscopically Assisted ACL Reconstruction. Orthopedics 18(3): 249-252, 1995.

#### DEPARTMENT OF SURGERY, UROLOGY SERVICE

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- Schwartz BF, Wettlaufer JN, Bagg MD, Thrasher JB The Normal Flora of the Human Epididymis. Infections Urology 7(6): 168, 1994.
- Sudduth RH The Effectiveness of Simethicone in Improving Visibility During Colonoscopy When Given With a Sodium Phosphate Solution: A Double-Blind Randomized Study. Gastrointest Endosc 42(5): 413-415, 95.

## INDEX TO PROTOCOLS

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**DETAIL SHEETS FOR PROTOCOLS**

**62ND MEDICAL GROUP**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/143		<b>Status:</b> On-going	
<b>Title:</b> Training of Veterinary Food Inspection Personnel in Field Slaughter and Inspection Methods Utilizing Domestic Swine (Sus scrofa domesticus)					
<b>Start Date:</b> 05/26/95			<b>Est. Completion Date:</b> Jun 96		
<b>Department:</b> 62nd Medical Group			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> C. H. Martinez					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Training:food inspection,Animal Study					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//	

Study Objectives: To train veterinary food inspection personnel in antemortem and postmortem inspection, dispatch, and field slaughter techniques.

Technical Approach: This training protocol will provide experience for food inspection personnel on techniques used within their occupation. A total of two domestic pigs will be used over a 6 month period. After being transported to the training area, the pigs will be inspected using recommended antemortem techniques, stunned using a captive bolt device or mallet and immediately exsanguinated. The methods used are approved by the AVMA Panel on Euthanasia and cause minimal pain or distress to the animals. The pigs will then be eviscerated and inspected using recommended postmortem techniques.

Progress : One session was held in FY95, and one animal was used.

**DETAIL SHEETS FOR PROTOCOLS**

**ACTIVE DUTY STUDENTS**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/136		<b>Status:</b> Completed	
<b>Title:</b> Electrical Stimulation and Diabetic Foot Skin Perfusion					
<b>Start Date:</b> 08/05/94			<b>Est. Completion Date:</b>		
<b>Department:</b> Active Duty Students			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Darlene M. Gilcreast, AN					
<b>Associate Investigators:</b>			Nancy A. Stotts, RN, Ed.D.		
<b>Key Words:</b> diabetes, foot, electrical stimulation					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		//

**Study Objective:** To examine the effect of electrical stimulation on skin perfusion of the feet in persons with diabetes who either have or are at risk for developing foot ulcers.

**Technical Approach:** Persons attending the Diabetic Foot Clinic at the California College of Podiatry Medicine will be invited to participate in the study. Persons consenting and meeting the entry criteria will have their oral temperature taken to rule out systemic infection.

For those in Wagner Grade 0 (intact skin), a table of random numbers will be used to select the study extremity. For those in Wagner Grades 1 and 2, the foot with the ulcer will be utilized. After baseline measurements are recorded, the electrical stimulation treatment will be initiated for a duration of 30 minutes. During the treatment, the nurse will monitor the patient and transcutaneous oxygen level readings will be taken and recorded at baseline, 15 minutes, 30 minutes and (end of treatment), and 60 minutes (30 minutes after the end of electrical stimulation). At the conclusion of the treatment, electrodes will be removed, wounds will be redressed as they were when the subject came in for study.

Double data entry will be used for computer analysis. A repeated measures, one-way analysis of variance will be performed to answer the primary hypothesis. Alpha is preset at 0.05. For each secondary hypothesis, a repeated measures, two-way analysis of variance will be performed. If significant, post-hoc analyses will be performed to examine the nature of the difference using the Scheffe test.

**Progress :** 135 subjects entered. Preliminary data indicates that some subjects respond to electrical stimulation by increased blood flow and the response continues through 30 minutes of recovery.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/082		<b>Status:</b> Completed
<b>Title:</b> The Effects of Rotating Shifts on Nurses in Military Hospitals				
<b>Start Date:</b> 05/06/94		<b>Est. Completion Date:</b> Jun 94		
<b>Departments:</b> Active Duty Students		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> M.L. Poso				
<b>Associate Investigators:</b>		Diane D. Stajduhar, RN		
<b>Key Words:</b> nurses:military, rotating shifts				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//

**Study Objective:** Describe the effects of shift work on nursing related to self reported accidents/medication errors in military hospitals.

**Technical Approach:** This study will use a survey to sample 300 nurse from 3 military medical centers. The relationship between rotating shifts and accidents/near accidents will be described through a self reported questionnaire.

Relationships between rotating shifts, sleep, and accidents will be computed using coerrelational formulas. The SPSS/PC+ statistical software will be used to compute data. A decision tree by Knapp will be sued to determine data analysis. Chi-square analysis of the associations of nominal data and T-test analysis of interval data is planned. Since some questions have multiple parts, more than one analysis may be used for a single question.

**Progress :** 200 surveys were mailed out. Responding nurses who rotated shifts reported more self-reported accidents then nurses who did not rotate. Nurses who rotated shifts reported shorter sleep periods and more sleepiness than nurses who did not rotate. Nurses who labeled themselves as evening types reported fewer accidents and near-accidents than nurses who labeled themselves as morning types.

**DETAIL SHEETS FOR PROTOCOLS**

**FORT LEWIS, SPECIAL FORCES**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/069	<b>Status:</b> On-going
<b>Title:</b> Special Operations Medical NCO Sustainment Training		
<b>Start Date:</b> 03/04/94	<b>Est. Completion Date:</b> Jun 96	
<b>Department:</b> Fort Lewis, Special Forces	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT G. Jeffrey Poffenbarger, MC		
<b>Associate Investigators:</b>	1LT Joseph R. James JR, MC	
<b>Key Words:</b> Training:medical, special operations,Animal Study		
<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	//

**Study Objective:** To support required annual Advanced Trauma Life Support type surgical training for all 18D Special Forces medical sergeants. To have exposure, gain experience, and develop proficiency in surgical procedures.

**Technical Approach:** The following surgical procedures will be performed: Endotracheal intubation, vessel cutdown and catheterization, Soft tissue handling/suturing, chest tube insertion, cricothyroidotomy, pericardiocentesis. All procedures will use goats and support staff from the Department of Clinical Investigation's Laboratory Animal Surgery Service. The trainees will be evaluated through visual observation of satisfactory skill level. Additionally, there will be a 2 day didactic course prior to the animal lab, which will culminate in a written test. After the animal lab all students will undergo a 20 minute oral exam on their performance and details of trauma medicine.

**Progress :** Two training session were done in FY 95. One involved 5 goats, the other 8 goats.

**DETAIL SHEETS FOR PROTOCOLS**

**U. S. DEPARTMENT OF AGRICULTURE**

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 92/001		<b>Status:</b> Ongoing
<b>Title:</b> Methods for Assessing Vitamin A Status in Healthy Adults				
<b>Start Date:</b> 10/04/91		<b>Est. Completion Date:</b> Jul 92		
<b>Department:</b> USDA		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Betty Jo Burri, Ph.D.				
<b>Associate Investigators:</b>		Andrew J. Clifford, Ph.D.		
<b>Key Words:</b> liver,vitamin A,isotope technique				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//

**Study Objective:** To determine vitamin A status in healthy free-living adults in the San Francisco area.

**Technical Approach:** This protocol will consist of studies focusing on three groups of people: (1) women aged 55-60 (2) men aged 55-60 and (3) men aged 18-24. Each group will consist of 30 healthy nonsmokers. These age and sex groups have been selected to include adults with divergent ages and because vitamin A and its analogs can be tetratogenic, making it potentially hazardous to administer analogs to young women. Subjects will be prescreened for serum retinol and holo-retinol binding protein (RBP) in an effort to get at least 15 people in each group with low vitamin A serum concentrations. Subjects will fill out a questionnaire in order to estimate their usual intake of high vitamin A foods over the past year. Body weights and blood pressures will be measured on the first and last days of the study. The vitamin A analogs are to be given on days one (didehydroretinol) and eight (tetradeuterated retinol acetate) of the study. In a pilot study to test the time course of equilibration and elimination of the analogs, three volunteers from each group will be given the cocktails as stated and blood samples taken a 5, 8, and 30 hr, and at 2, 3, 4, 5, 15 days and every 30 days thereafter. This blood would be collected in addition to the blood required for the regular study (pre ingestion, 5 hr, and days 8, 29, and 30). The study will compare three promising new methods for assessing vitamin A status to serum retinol, and to vitamin A liver stores measured by deuterated analogs and by vitamin A2. The new methods tested will be free- and transthyretin-bound holo-retinol binding protein as determined by HPLC, erythrocyte transglutaminase levels, and goblet cell abnormalities. Addendum (Oct 91): All of the testing was done except for tests of the vitamin A2. Vitamin A2 proved to be very difficult to purify, so it was never actually given to the subjects. Then two significant things happened a supply of high quality vitamin A2, approved for human use, was obtained, and it was found that the tetradeuterated analog may interfere with the vitamin A2 test, even when these analogs are given 8 days apart. It is now recommended that the doses of vitamin A2 and other analogs be separated by at least 30 days. Therefore in this study, the vitamin cocktails will be given on day 1 and day 30, with blood draws added as appropriate.

**Progress :** Enrollment stands at 54. Participants will be contacted for follow-up shortly.

**DETAIL SHEETS FOR PROTOCOLS**

**BEHAVIORAL HEALTH SCIENCE**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/108		<b>Status:</b> On-going	
<b>Title:</b> Medical Cost Offset and Clinical Effectiveness of a Behavioral Treatment Program for Medical Resource Overutilizers					
<b>Start Date:</b> 05/06/94			<b>Est. Completion Date:</b> Jan 96		
<b>Department:</b> BHS			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC John B. Powell, MS					
<b>Associate Investigators:</b> C. Ellsworth			M. Brencick A.M. Thorndyke		
<b>Key Words:</b> medical resources, overuse, treatment program					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> //

**Study Objective:** This study will identify patients with few physical findings and whose presenting complaints are produced or aggravated by psychological, rather than organic, factors, and to provide a brief, effective behavioral intervention designed to ameliorate these psychological factors.

**Technical Approach:** This study will follow 100 patients referred from the Adult Primary Care Center, and compare them to 100 non-treatment controls. Patients will complete a four week behavioral program consisting of four weekly classes and four individual biofeedback sessions. medical usage for the six months prior to treatment (including outpatient visits, inpatient treatment, laboratory procedures, and pharmacy costs) will be compared to usage for the six months post treatment.

**Progress :** 525 patients have been enrolled. A sub-sample of patients who completed the program or who were never treated were evaluated extensively for medical utilization rates for the 6 months pre- and post-treatment. Significant reductions from baseline in medical utilization were found for the treatment group (23% decrease in outpatient, 72% decrease in inpatient, and similar reductions in lab & pharmacy; radiology was not significant due to two outliers). The non-treatment group showed substantial increases in utilization over baseline, but cannot be considered an adequate control group because of selection biases. A new method for defining a control group based upon medical utilization rates is being explored with Coordinated Care Division.

## Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 95/013

**Status:** On-going

**Title:** Effect of Premenstrual Syndrome and Primary Dysmenorrhea on Women's Cognitive Functioning and Job Performance Before and After Biofeedback Treatment

**Start Date:** 11/04/94

**Est. Completion Date:** Sep 95

**Department:** BHS

**Facility:** MAMC

**Principal Investigator:** LTC John B. Powell, MS

**Associate Investigators:**

J. Norris  
M. Hibbert

COL Gary D. Davis, MC  
C.J. Sherman  
LTC Richard A. Sherman, MS

**Key Words:** Premenstrual syndrome, dysmenorrhea, cognitive functioning, job performance, biofeedback

Accumulative	Est. Accumulative	Periodic Review:
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	//

**Study Objectives:** To determine whether PMS and dysmenorrhea: (1) have a significant impact on the job performance of those female soldiers who do and those who do not request treatment for these problems, and; (2) have a significant impact on the cognitive functioning of female soldiers who request treatment, and, if this correlates highly with changes in work performance. Also, to determine whether biofeedback intervention will make a significant impact on the work performance of female soldiers who request treatment by producing about a 50% reduction in pain among about 80% of those requesting treatment. Lastly, to determine whether females given biofeedback training for PMS and dysmenorrhea who do not successfully complete their training will not show a change in the intensity of their symptoms from before to after training.

**Technical Approach:** We propose to determine the impact of primary PMS and dysmenorrhea on female soldiers's performance of the normal duties and whether treatment with biofeedback alters the impact. Impact will be assessed by having 200 female soldiers form combat service and combat service support units requesting treatment for either PMS or dysmenorrhea keep deep daily, month long logs of their symptom activity, medication use, and limitations to their performance. One month is the minimum length log acceptable because of the cyclic nature of the problems in relation to the menstrual cycle. Each of these women will also take an hour long, automated cognitive screening evaluation twice. One evaluation will be during the highest level of their symptoms and the other will be at the lowest level. This will permit correlations of changes in cognitive processing with changes in work performance. Two hundred female soldiers not requesting treatment for these problems who are matched with the soldiers requesting treatment for medical history, family life style, and job type will also be asked to keep a log to control for aspects of military life affecting job performance unrelated to PMS and dysmenorrhea. This control group will be large enough to estimate the impact of these problems on job performance among female soldiers since about 15% of young adult civilian women report significant problems with PMS or dysmenorrhea. Participants will be recruited from the appointment lists at MAMC's clinics and the TMCs. The time period between when they make their appointments, through the wait to see a doctor, and the time their first trial medications take effect will permit participants to keep their one month logs before their symptom activity is impacted by any new treatments.

**Progress :** 178 subjects were entered. Results indicate that 23% report significant symptoms of PMS, 8% report significant dysmenorrhea, and 24% report a combination of both. Only two subjects have completed the treatment phase.



**DETAIL SHEETS FOR PROTOCOLS**

**BEHAVIORAL HEALTH SCIENCE, CLINICAL**  
**PSYCHOLOGY SVC**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/130		<b>Status:</b> On-going	
<b>Title:</b> MMPI-2 Profiles in Korean Military Dependents					
<b>Start Date:</b> 06/16/95			<b>Est. Completion Date:</b> Aug 95		
<b>Department:</b> BHS, Clinical Psychology Svc			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Kathleen S. Lester, MS					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Military dependents:Korean-born, MMPI-2					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//	

**Study Objectives:** To determine the normative scores for the Minnesota Multi-phasic Personality Inventory-2 (MMPI-2) in Korean dependent wives of active duty soldiers.

**Technical Approach:** In order to determine the norms for the Korean female spouses of service members, the MMPI-2 will be administered to 50 subjects, age 20 to 70. Subjects will be recruited from the primary care clinics at MAMC by means of referral by their physician and through recruitment advertisements posted in community areas of Ft. Lewis. Subjects consenting to participate will be given a questionnaire, a brief, structured psychiatric interview (mini-SCID), a screening test of English proficiency and the MMPI-2. The mean and standard deviation of the clinical and validity scales will be derived for the group. These scores will be compared with existing norms and, where differences exist, t-tests of significance will be performed. Results will be examined for co-variance of factors of age, number of years in the U.S, and proficiency in English language.

**Progress :** 8 subjects entered. Subjects continue to be recruited.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF CLINICAL INVESTIGATION**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/103		<b>Status:</b> On-going	
<b>Title:</b> Polymerase Chain Reaction Detection and Cell Culture of Herpes Simplex Virus from Urine of Symptomatic Males with Non-gonococcal Urethritis					
<b>Start Date:</b> 04/21/95			<b>Est. Completion Date:</b> Oct 95		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Wade K. Aldous, MS					
<b>Associate Investigators:</b> MAJ Darrell E. Griffin III, MS			MAJ Margot R. Krauss, MC		
<b>Key Words:</b> Herpes simplex, polymerase, non-gonococcal urethritis					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		//	

**Study Objective:** To determine the feasibility of using a urine sample for detection and culture of Herpes Simplex Virus (HSV) in patients suspected of having non-gonococcal urethritis (NGU) due to HSV.

**Technical Approach:** Twenty males presenting with HSV And NGU will be tested for evidence of HSV infection in the urethra. Urine will be submitted from the Dept. of Pathology to the Dept. of Clinical Investigation for analysis. Cells will be collected from the urine by centrifugation and processed for cell culture and for detection by the polymerase chain reaction (PCR) using primers specific for HSV. Results of cell culture will be compared with PCR results. Samples positive for both culture and PCR will be considered true positives and thus will determine the feasibility of using urine samples for HSV detection in NGU patients. This is a descriptive study of a new technique.

**Progress :** 10 out of 20 subjects have been entered so far. We have not been able to culture out HSV from any of the subjects thus far, but using a spike urine sample, HSV can survive in the urine for a short time period. We have been saving samples for fluorescent antibody staining as well as for polymerase chain reaction detection of amplified HSV DNA when all 20 can be performed simultaneously

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/156		<b>Status:</b> Terminated	
<b>Title:</b> Isolation, Purification, and Characterization of Telomerase from Human Breast Cancer					
<b>Start Date:</b> 07/21/95			<b>Est. Completion Date:</b>		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Wade K. Aldous, MS					
<b>Associate Investigators:</b> Louis A. Matej, B.S.			Katherine H. Moore, Ph.D. James R. Wright, M.T.		
<b>Key Words:</b> Cancer:breast, telomerase					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> //

Study Objective: The objectives of this project are threefold: 1) Extraction and isolation of telomerase from breast cancer cells. 2) Purification of telomerase by affinity chromatography. 3) Characterization of purified telomerase as achieved by polyacrylamide gel electrophoresis, protein sequencing, and possible subcloning of individual telomerase components.

Technical Approach: The study is designed to isolate and purify telomerase from a known breast cancer cell line MCF-7. The enzyme telomerase is a ribonucleoprotein consisting of protein and RNA components. The RNA component is complementary to the telomeric repeat sequence TTAGGG. The enzyme will be extracted from cultured cells and tested for activity. Active enzyme will be further purified by affinity chromatography, utilizing a portion of the telomeric repeat sequence GATTGGGAT attached to a solid support by a linker arm. This purified extract will again be tested for telomerase activity to ensure a functional enzyme.

Telomerase activity will be determined using the enzyme's ability to add 6 bp tandem repeats (TTAGGG) to an initial DNA fragment. By using a radiolabeled nucleotide, the tandem repeats can be visualized autoradiographically as a ladder.

Telomerase can then be characterized by polyacrylamide gel electrophoresis under denaturing and non-denaturing conditions which will show the relative size of the enzyme and whether or not there are subunits. A two-dimensional acrylamide gel can be used to separate fragments even more, which will enable individual fragments to be sequenced using an amino acid sequencer. Any amino acid sequence determined can be further used to clone fragments of telomerase.

Progress : This protocol is still in the planning stages. An article was recently published that discussed the isolation and characterization of human telomerase positive cell lines (very similar to what was planned for this study).

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/157		<b>Status:</b> Terminated	
<b>Title:</b> Isolation, Purification, and Characterization of Telomerase from Human Germ-Line Cells					
<b>Start Date:</b> 07/21/95			<b>Est. Completion Date:</b> Sep 97		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Wade K. Aldous, MS					
<b>Associate Investigators:</b> CPT Raymond S. Lance, MC Louis A. Matej, B.S.			Katherine H. Moore, Ph.D. CPT Jason L. Blaser, MS James R. Wright, M.T.		
<b>Key Words:</b> Cancer:germ-cell, telomerase					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		//	

**Study Objective:** The objectives of this project are three fold: 1) Extraction and isolation of telomerase from human germ-line cells. 2) Purification of telomerase by affinity chromatography. 3) Characterization of purified telomerase as achieved by polyacrylamide gel electrophoresis, protein sequencing, and possible subcloning of individual telomerase components.

**Technical Approach:** The study is designed to isolate and purify telomerase from a human germ-line cells from testes. The enzyme telomerase is a ribonucleoprotein consisting of protein and RNA components. The RNA component is complementary to the telomeric repeat sequence TTAGGG. The enzyme will be extracted fro cultured cells and tested for activity. Active enzyme will be further purified by affinity chromatography, utilizing a portion of the telomeric repeat sequence GATTGGGAT attached to a solid support by a linker arm. This purified extract will again be tested for telomerase activity to ensure a functional enzyme.

Telomerase activity will be determined using the enzyme's ability to add 6 bp tandem repeats (TTAGGG) to an initial DNA fragment. By using a radiolabeled nucleotide, the tandem repeats can be visualized autoradiographically as a ladder.

Telomerase can then be characterized by polyacrylamide gel electrophoresis under denaturing and non-denaturing conditions which will show the relative size of the enzyme and whether or not there are subunits. A two-dimensional acrylamide gel can be used to separate fragments even more, which will enable individual fragments to be sequenced using an amino acid sequencer. Any amino acid sequence determined can be further used to clone fragments of telomerase.

**Progress :** This protocol is still in the planning stages. An article was recently published that discussed the isolation and characterization of human telomerase positive cell lines (very similiar to what was planned for this study).

### Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 94/084

**Status:** On-going

**Title:** Veterinary Support Personnel and Investigator Training in Animal Care Procedures (Swine *Sus scrofa*, Goat *Capra hircus*, Rabbit *Oryctolagus cuniculus*, Ferret *Mustela putorius furo*, Rat *Rattus* ...

**Start Date:** 02/09/94

**Est. Completion Date:** Feb 97

**Department:** Clinical Investigation

**Facility:** MAMC

**Principal Investigator:** CPT Stephen Caldwell, VC

**Associate Investigators:** None

**Key Words:** Training:vet techs,Animal Study

**Accumulative**

**Est. Accumulative**

**Periodic Review:**

**MEDCASE Cost:** \$0.00

**OMA Cost:** \$200.00

//

**Study Objective:** 1) To help the DCI technical staff to remain proficient in basic technical skills as well as emergency care procedures that may arise during normal animal care. 2) To teach investigators and technicians the basics of animal restraint and manipulations. 3) To teach DCI technical staff basic surgical skills that will enable them to better assist investigators.

**Technical Approach:** The DCI technical staff trainees will be instructed in proper handling and restraint techniques used with the Swine *Sus scrofa*, Goat *Capra hircus*, Rabbit *Oryctolagus cuniculus*, Ferret *Mustela putorius furo*, Rat *Rattus norvegicus*, and Mouse *Mus musculus*. Trainees will be taught basic surgical skills, to include endotracheal intubation; blood collection and injections; vessel cutdown and catheterization; soft tissue handling and suturing; anesthetic regimens, and necropsy procedures.

**Progress :** No classes were held in FY 95.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/025		<b>Status:</b> On-going	
<b>Title:</b> The Department of Clinical Investigation's Molecular Biology Short Course for Physicians					
<b>Start Date:</b> 12/16/94			<b>Est. Completion Date:</b> Jun 96		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Rodger K. Martin, MS					
<b>Associate Investigators:</b>			CPT Wade K. Aldous, MS		
<b>Key Words:</b> Molecular biology, training course					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		//	

**Study Objectives:** To familiarize MAMC residents, fellows, and staff physicians with the research capabilities and resources of the Department of Clinical Investigation. To support MAMC Graduate Medical Education through instruction and research. To foster an appreciation of molecular biology concepts in residents, fellows, and staff physicians and to augment their understanding of the scientific literature. To encourage residents, fellows and staff physicians to develop research protocols incorporating these technologies.

**Technical Approach:** This course is designed to familiarize physicians with the most commonly encountered molecular approaches in the scientific and clinical literature. It is hoped that this will foster more critical reading of the literature as well as encouraging the development of research protocols employing these technologies. Although six weeks in duration, students will be required to attend two hours of lecture per week in addition to approximately seven hours of laboratory exercises. Topics addressed and used in the course range from DNA isolation to cloning and sequencing of PCR products.

**Progress :** DCI sponsored two iterations of the highly acclaimed Molecular Biology Short Course for Physicians in FY95. Twelve physicians were trained in basic molecular biology skills. The Spring '95 course targeted primarily MAMC staff physicians. Six physicians were enrolled and completed the course which included approximately 48.5 hours of didactic and hands-on training in molecular biology. The course director was CPT Martin and the assistant course director was CPT Aldous. The Fall '95 course also had six physicians enrolled. In contrast to the Spring course, priority was given to fellows, residents and staff members in that order. CPT Aldous was the course director.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/079		<b>Status:</b> On-going	
<b>Title:</b> The Detection of Atrial Natriuretic Peptide and Neutral Endopeptidase mRNA from Placentas in Normal and Pre-eclamptic Pregnancies					
<b>Start Date:</b> 03/04/94			<b>Est. Completion Date:</b> May 94		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Rodger K. Martin, MS					
<b>Associate Investigators:</b>			MAJ Glenn R. Markenson, MC		
MAJ Katherine S. Foley, MC			LTC Arthur S. Maslow, MC		
MAJ Jerome N. Kopelman, MC					
<b>Key Words:</b> mRNA, atrial natriuretic factor, endopeptidase, placenta					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		//	

Study Objective: To ascertain the presence of mRNA for atrial natriuretic factor (ANF) and neutral endopeptidase (NEP) in placental tissues.

Technical Approach: Three placentas from uncomplicated, term deliveries and three placentas from pregnancies complicated by pre-eclampsia will be obtained. RNA will be extracted from samples of the umbilical artery and vein, the amnion and chorion, and decidua plate. The presence of ANF or NEP mRNA will be ascertained by northern analysis, RNase protection assay (RPA), or by the reverse transcriptase-polymerase chain reaction (RT-PCR). Samples of the placental tissues will be evaluated by electron microscopy to search for granules similar to those in the cardiac atria, that contain ANF.

Progress : A total of 6 placentas were studied; three from uncomplicated term pregnancies, and three from pregnancies complicated by proteinuric preeclampsia. The newly designed primers revealed positive results in both human and placental tissues. However, in placentas from the pre-eclamptic pregnancies, RT-PCR detected ANF production in the chorionic tissues.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/012		<b>Status:</b> On-going	
<b>Title:</b> The Relationship of Bacterial Contamination and Interleukin-6 in Amniotic Fluid in Preterm Labor and Delivery					
<b>Start Date:</b> 11/04/94			<b>Est. Completion Date:</b>		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Rodger K. Martin, MS					
<b>Associate Investigators:</b> MAJ Katherine S. Foley, MC			MAJ Glenn R. Markenson, MC M.K. Yancy		
<b>Key Words:</b> Pregnancy: bacteria, inerleukin-6, amniotic fluid					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		//	

**Study Objectives:** To determine the differences in gestational length of pregnancies complicated by preterm labor with and without bacteria in the amniotic fluid as detected by the polymerase chain reaction (PCR). To ascertain the relationship between the presence of bacteria detected using the PCR and elevated concentrations of interleukin-6 (IL-6) in amniotic fluid from preterm deliveries.

**Technical Approach:** One hundred and fifty women requiring amniocentesis will be enrolled in this collaborative project at the Madigan and the Tripler Army Medical Centers. Amniotic fluid from pregnancies complicated by preterm labor will be obtained only in clinically indicated situations that require analysis to rule out chorioamnionitis. Amniotic fluid will be evaluated for the presence of bacteria utilizing the PCR to amplify a ribosomal consensus sequence of DNA in bacteria. The presence of such sequences in amniotic fluid will be considered as evidence of bacterial contamination. At the time of amniocentesis the fluid will be gram stained and cultured for aerobic and anaerobic bacteria. the fluid obtained will also be evaluated for IL-6 concentration. After delivery, placentas will be sent to pathology. The presence of polymorphonuclear cell in formalin-fixed, paraffin-embedded chorion or amnion will be evidence for chorioamnionitis. The relationship of the outcomes of these tests to preterm delivery will then be assessed as well as the relationship between elevated IL-6 levels and positive PCR studies.

**Progress :** Sixty-six women have been enrolled in this study from MAMC and TAMC. The cubacterial primers are very sensitive for the detection of bacteria. Using PCR, samples as dilute as <50 bacteria per ml have been detected in bacterial spiked saline samples. Anticipate beginning the batch interim analysis on the amniotic fluid samples by mid July 96.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/169		<b>Status:</b> On-going	
<b>Title:</b> Development of a Method to Study What Proteins Are Regulated by IGF in the PC3 Prostate Cancer Cell Line Using 2-D Gel Electrophoresis and Protein Sequencing					
<b>Start Date:</b> 09/21/94			<b>Est. Completion Date:</b>		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Louis A. Matej, B.S.					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> cancer:prostate, cell line, protein regulation, IGF					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		//	

**Study Objective:** The objective of this study is to develop a method for using a 2-D Electrophoresis coupled with Protein Sequencing to quantitate and identify proteins produced or inhibited by PC3 Prostate Cancer Cells when regulated by IGF.

**Technical Approach:** PC3 prostate cancer cells will be grown to confluency at 37°C in RPMI media supplemented with 5% Fetal Bovine Serum and in a 6% humidified CO<sub>2</sub> atmosphere. One culture will be inoculated with IGF at 10<sup>-6</sup>M; another culture will serve as a normal control. In the media of both the regulated and non-regulated PC3 prostate cell cultures, C<sup>14</sup> labeled amino acids will be added to allow in the detection of proteins by autoradiography. The cultures will be allowed to incubate for 48 hours.

The media will be pipetted and saved to further study extracellular proteins while the cells will be trypsinized, sonicated in lysing buffer, and the mixture ultracentrifuged to acquire intracellular proteins for further study. The investigator plans to isolate and wash the protein from these solutions by using a dot blot apparatus to bind proteins to a nitrocellulose membrane. The proteins can then be desalted and washed on the membrane. To extract the proteins off the nitrocellulose membrane, we will use 8 M urea in sample buffer.

The IEF (1st dimension) electrophoresis which separates protein by isoelectric point will be carried out using polyacrylamide tube gels having equal amounts of ampholyte pH range 4.0-6.0, ampholyte pH range 6.0-8.0 and ampholyte pH range 7.0-9.0.

The second dimension electrophoresis, which separates protein further by size, will be carried out by layering the tube gel onto a vertical 10 to 20 percent gradient polyacrylamide gel.

The investigator will transfer the proteins onto a PVDF membrane by using an electroblot apparatus followed by staining with coomassie blue and destaining with a methanol/acetic acid/water solution. Autoradiography will then be used to allow more sensitive identification of protein bound to the PVDF membrane. After visual, graphic, and computer analysis of the autoradiographs, purified protein spots will then be cut out of the membrane and sequenced using the ABI protein sequencer. The protein sequences will be used to compare quantities of each protein of interest as well as for identification of the protein.

**Progress :** No work has been done on this protocol due to time restraints of the principal investigator.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 87/100		<b>Status:</b> On-going
<b>Title:</b> Thyroid Size in Children and Adolescents				
<b>Start Date:</b> 08/21/87		<b>Est. Completion Date:</b> Nov 91		
<b>Department:</b> Clinical Investigation		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL Dan C. Moore, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> thyroid size,adolescents				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	09/16/88

**Study Objective:** To establish normal dimensions  $\pm 2$  standard deviations (SD) for thyroid lobe length and width in children and adolescents. A goiter would then be defined as thyroid gland exceeding 2 SD of these dimensions.

**Technical Approach:** During the course of a routine physical examination, thyroid glands of 300 normal children and adolescents aged 6-20 years (20 at each age, 10 of each sex) will be measured in the following manner. With the neck extended, the thyroid isthmus is located with the index finger. The medial aspect of each lobe is followed to the apparent tip of each lobe. The upper tip of each lobe is located as the patient swallows with the index finger over each tip. The apparent inferior border of each lobe is located as the patient swallows with the index finger over the inferior portion of the gland. The lateral borders of the gland will be located with the index fingers placed medial to the sternocleidomastoid muscle as the gland moves as the patient swallows. The length will be measured as the distance from the apparent tip of each lobe to the apparent inferior border of each lobe. The width will be measured as the distance from the lateral borders of the gland. Means and SD will be calculated for length of each lobe and mid-isthmus width. For validation of measurement accuracy, 30 patients (2 each age, 1 each sex) will have the same measurements determined by thyroid ultrasound.

**Progress :** 393 subjects have been enrolled in this study. Data collection continuing. Preliminary analysis shows a difference in thyroid size by pubertal stage and correlates with body mass index.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 90/091		<b>Status:</b> On-going
<b>Title:</b> A Phase III Open Protocol for a Multicenter Study for the Treatment of Central Precocious Puberty with D-Trp(6)-Des-Gly(10)-N-ethylamide-LHRH, A Long-Acting Analog of Luteinizing Hormone Releasing....				
<b>Start Date:</b> 07/20/90		<b>Est. Completion Date:</b> Nov 92		
<b>Department:</b> Clinical Investigation		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL Dan C. Moore, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> precocious puberty,deslorelin,LH				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>
\$0.00		\$0.00		07/21/95

**Study Objective:** To treat patients who have central precocious puberty with Deslorelin in order to suppress pubertal development and excess growth, to restore gonadotropin and sex hormone levels to normal prepubertal levels, and to demonstrate the safety of such treatment.

**Technical Approach:** Central precocious puberty will be defined as: stage 2 pubic hair or greater, stage 2 breast or genital development or greater, pubertal LH and FSH peak following GnRH stimulation, and absence of peripheral origin of precocity (lack of adrenal or ovarian mass on ultrasound and normal serum hCG). After diagnosis and standard evaluations, patients will be given Deslorelin, 4 mcg/kg SC daily. At three month intervals, patients will be re-evaluated. A physical examination with pubertal staging will be done. Serum sex hormones and gonadotropins (before and after GnRH) will be measured and bone age will be determined. Treatment will be continued until the patient reaches an age at which pubertal development is deemed appropriate (usually 10-11 years) at which time therapy will be discontinued.

**Progress :** Three subjects have been enrolled in this study. One patient died due to underlying disease. One patient remains in this study. Study drug continues to be effective in preventing puberty.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/003		<b>Status:</b> On-going	
<b>Title:</b> Characterization of the Genetic Basis for the Syndrome of Hypoparathyroidism, Deafness, and Renal Hypoplasia					
<b>Start Date:</b> 10/01/93			<b>Est. Completion Date:</b> Apr 94		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL Dan C. Moore, MC					
<b>Associate Investigators:</b>			CPT Rodger K. Martin, MS		
<b>Key Words:</b> hypoparathyroidism, deafness, renal hypoplasia, DNA					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$1200.00	//	

**Study Objective:** Using techniques of DNA isolation, PFLP analysis, Southern analysis and probing with cDNA sequences of interest, to identify in chromosome 11, (which contains the PTH gene), genetic variation that is associated with the extremely rare syndrome of hypoparathyroidism, deafness and renal hypoplasia, which has been diagnosed in a family treated by the principal investigator. To date, no genetic etiology for this syndrome has been elucidated.

**Technical Approach:** Blood will be obtained from a patient with the syndrome of hypoparathyroidism, deafness and renal hypoplasia and from as many family members as possible. Because of the rarity of the syndrome and the non availability of the family locally, lymphocytes will be transformed with EB virus to provide a constant source of genomic DNA. Genomic DNA will be isolated from subjects' lymphocytes, digested with a series of endonucleases and RFLP analysis done, seeking genetic variants that segregate with the patient's restriction fragment digest. Restriction fragment digests will be transferred to membranes for Southern analysis and probed with labelled cDNA probes corresponding to sequences of interest on chromosome 11.

**Progress :** Currently, a method for immortalization of lymphocytes if being perfected so that DNA can be harvested for analysis.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 91/092		<b>Status:</b> Terminated	
<b>Title:</b> Characterization of LH Isoforms in Treated and Untreated Precocious Puberty					
<b>Start Date:</b> 09/06/91			<b>Est. Completion Date:</b> Jun 92		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL Dan C. Moore, MC					
<b>Associate Investigators:</b> MAJ Jim Hansen, MC			Katherine H. Moore, Ph.D.		
<b>Key Words:</b> precocious puberty,LH:isoforms					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$1843.00		//	

Study Objective: To determine the luteinizing hormone (LH) isoform pattern in precocious puberty and demonstrate whether there is a change in isoform pattern during therapy with gonadotropin-releasing hormone (GnRH) analogue (leuprolide) and to confirm whether changes in LH bioactivity correlate with parallel changes in LH isoform pattern during therapy.

Technical Approach: This is a collaborative study using serum obtained from subjects in the University of Iowa protocol entitled "New Treatments to Improve the Final Height of Children with Central Precocious Puberty". Paired frozen sera from 12 subjects, will be processed as follows: 1 ml of serum will be dialyzed against two changes of 2 liters of 0.025 M Tris (pH=9.3) for 2 hours and then applied to a 1.0 x 20 cm Mono P HR 5/20 column (4 ml column volume), which has been equilibrated with 15 column volumes of 0.025 M Tris (pH=9.3). The sample is eluted with 50 ml Polybuffer 96 (diluted 1:10 with water, pH=6.0) at 1 ml/min and collected in 2 ml fractions. To study LH isoforms which are present between pH 7 and 4, similar procedures will be used, substituting Polybuffer 74 and Tris protein precipitation with 0.5 ml of 1% BSA and 2.8 g of powdered ammonium sulfate. After thorough mixing and incubating at 20 deg C for 2 hr., the fractions are centrifuged at 1500 g for 30 minutes. Supernatant is discarded and precipitates are washed once with saturated ammonium sulfate and then reconstituted in 0.5 ml of assay buffer for LH RIA and bioassay. Aliquots of fractions which contain LH activity will be pooled for each chromatofocusing peak and analyzed for LH immunoactivity and bioactivity. Changes in bioactivity correlating with changes in chromatofocusing pattern will be sought in pre and post treatment sera.

Progress : This study was terminated because LH fractions were not measureable by mouse LH bioassay.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 92/048		<b>Status:</b> On-going	
<b>Title:</b> Treatment use of Oxandrin (Oxandrolone) in Boys with Constitutional Delay of Growth and Puberty					
<b>Start Date:</b> 04/03/92			<b>Est. Completion Date:</b>		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL Dan C. Moore, MC					
<b>Associate Investigators:</b>			LTC Robert A. Newman, MC		
<b>Key Words:</b> delayed maturation and growth, boys, oxandrin					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		08/18/95	

**Study Objective:** To provide a means by which boys with constitutionally delayed growth and puberty can be treated with oxandrolone secondarily, data will be collected regarding the effect of therapy on growth and also of significant importance, boys receiving oxandrolone will be monitored for evidence of drug-induced side effects.

**Technical Approach:** Boys with constitutional delay of growth and puberty will receive oxandrolone orally as prescribed by the physician. The recommended daily dose based on the published medical literature is up to 0.1 mg/kg. The duration of oxandrolone therapy will be left to the discretion of the physician. However, the published medical literature reports the safe and effective use of oxandrolone at the recommended doses for 3 to 12 months. The primary determinants for cessation of therapy are (1) inappropriate skeletal maturation (2) failure of drug to produce desired effect (3) spontaneous Stage III pubertal development as evidenced by a testicular volume of >10 ml or a length (long axis) of >3.5 cm or (4) adverse effects. Clinic visits not less than every four months will include interval medical history clinical side effects and adverse drug events and a pertinent physical examination. Bone age analysis, hemoglobin, hematocrit, RBC, and IGF-I (somatomedin-C) will be done at baseline, at 6 and 12 months, and annually thereafter.

**Progress :** This is a treatment protocol with very strict criteria. No suitable subjects have been identified.



### Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 95/081

**Status:** On-going

**Title:** Genentech National Cooperative Growth Study (NCGS) Post Marketing Surveillance Program for Protropin (Somatrem for Injection) and Nutropin (Somatropin [rDHA Origin]) for Injection)

**Start Date:** 03/17/95

**Est. Completion Date:** Dec 04

**Department:** Clinical Investigation

**Facility:** MAMC

**Principal Investigator:** COL Dan C. Moore, MC

**Associate Investigators:**

LTC Robert A. Newman, MC

**Key Words:** Growth:delay, Protropin, Nutropin

**Accumulative**

**Est. Accumulative**

**Periodic Review:**

**MEDCASE Cost:** \$0.00

**OMA Cost:** \$0.00

//

**Study Objective:** To collect long-term safety and efficacy information regarding treatment of children who have growth failure due to a lack of endogenous growth hormone secretion with Protropin and/or Nutropin growth hormone (GH).

**Technical Approach:** This is a multi-center, open label, post-marketing surveillance study of Protropin and Nutropin in the United States and Canada. Patients are enrolled at the time of their initiation of Protropin or Nutropin therapy and followed throughout their course of therapy. Post-treatment height measurements are collected until adult height is achieved. Since this is a record review and data collection only protocol, the number of patients enrolled will depend on the number requiring treatment for standard medical indications.

**Progress :** No subjects have been entered due to the fact that MAMC has switched to use of Humatrope instead of Protropin or Nutropin.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/044		<b>Status:</b> On-going	
<b>Title:</b> The Biologic and Genetic Identification of Risk Factors in Breast Lesions and Breast Cancer for Their Clinical Application in the Care of Military Women					
<b>Start Date:</b> 02/17/95			<b>Est. Completion Date:</b> Dec 96		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Katherine H. Moore, Ph.D.					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Cancer:breast, military women					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//	

**Study Objectives:** To develop methods to study two potential genetic lesions in breast cancer and pre-cancerous breast lesions. The two genetic lesions of interest are *HER2/neu* and *p53*. To also determine if risk predictors, *HER2/neu* and *p53* mutations can be detected in pre-malignant and early stage breast cancer tissue. This data will be used to support a grant application in which the goal will be to determine if examination of biopsy tissue for genetic lesions provides clinically important information for the treatment of breast disease.

**Technical Approach:** Amplification of the *HER2/neu* and mutations of *p53* oncogenes have been associated with poor prognosis in breast cancer. The types of cancers that have been studied, however have tended to be when the cancer has progressed to an advanced stage. We wish to determine if these genetic lesions are present in pre-cancerous lesions and be associated with a reoccurrence of aggressive disease in the same patient in the future. The major problem with doing genetic tests on precancerous lesions is the lack of tissue for conventional genetic analysis (southern blotting, RFLP analysis). The advent of PCR based technology has made the study of small lesions feasible. To develop genetic assays for the amplification of *HER2/neu* and mutations in *p53*, DNA will be isolated from breast cancer cell lines, including MCF-7, ZR-75-1 and SK-BR-3. The technique of differential PCR will be used to determine gene amplification of *HER2/neu*. A 98 bp portion of the *HER2/neu* gene and a 150 bp portion of a reference gene, interferon  $\gamma$ , will be amplified in the same reaction. The level of amplification of *HER2/neu* is reflected by the ratio between the *HER2/neu* PCR product and the  $\gamma$  interferon PCR product. Two methods will be used to detect mutations in *p53* DNA. One is single strand conformational polymorphism (SSCP), in which small changes in DNA sequence are detectable by changes in PCR fragment mobility of an acrylamide gel. The other method will be direct DNA sequencing of the PCR products. An automated DNA sequencing system (ALF, Pharmacia) will be used for these analyses.

**Progress :** Two oncogenes have been identified for the purposes of this study, *Her2/neu*, and *p53*. The assays to detect these two genetic lesions are being developed for our laboratory. The *Her1/new* assay uses differential PCR to detect gene amplification. We are using chemiluminescent methods to increase the sensitivity and speed of this test. We are detecting *p53* mutations by using PCR amplification of DNA, and SSCP followed by DNA sequence analysis to characterize the site of mutation,.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/126		<b>Status:</b> On-going	
<b>Title:</b> Sex Hormone Binding Globulin and Prostate Cancer - Characterization of Alternate mRNA Transcripts					
<b>Start Date:</b> 05/19/95			<b>Est. Completion Date:</b> Jul 97		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Katherine H. Moore, Ph.D.					
<b>Associate Investigators:</b> Louis A. Matej, B.S.			CPT Wade K. Aldous, MS M. J. Styner, B.S.		
<b>Key Words:</b> Cancer:prostate, SEBG, mRNA transcripts					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//	

**Study Objective:** Our first objective is to characterize the sex hormone binding globulin (SHBG) mRNA produced by prostate cancer cells. This will be accomplished by characterizing the SHBG products amplified by PCR, and ultimately the full length transcripts. Our second objective is to determine if SHBG mRNA is translated into protein. This will be accomplished by metabolically labeling the proteins in the cells and detecting by immunoprecipitation. A long range objective is to develop an antibody against the protein product of an altered SHBG mRNA, and use this antibody to determine if the proposed altered transcript is translated into functional protein.

**Technical Approach:** SHBG is a high affinity binding protein for androgens and estrogens. This protein is normally produced in the liver, released into the blood and functions to regulate the amount of free androgen or estrogen available for action at target organs. Recently, receptors for SHBG have been identified on prostate carcinoma cells. Prostate cancer is generally considered to be modulated by steroids. One proposed consequence of the SHBG receptor on cancer cell is the additional targeting of steroid to the cell. SHBG may have a role independent of steroid action and may be a growth factor itself. We will examine prostate cancer cell lines for the presence of SHBG mRNA. In addition, we will construct a cDNA library to fully characterize the SHBG transcripts produced by prostate cancer cells. We plan to examine the proteins manufactured by prostate cancer cell using immunoprecipitation to determine if the cells are producing SHBG protein. This study will thus characterize a potential oncogene for prostate cancer and lead to a greater understanding of the mechanism of cancer formation. This is a descriptive study. The DNA sequences will be compared with known sequences using MacVector.

**Progress :** Total RNA was extracted from two prostate cancer cell lines, DU-145 and PC3, and from cultured prostate epithelial and fibroblast cells. The reverse transcriptase polymerase chain reaction (rtPCR) was used to amplify the region of the SHBG mRNA spanning exon 5 to exon 8. This region was of interest as we have found alternatively spliced SHBG mRNAs in breast cancer cells using this set of primers. The PCR products were probed with a 550 bp probe that spans this region. The PCR fragments from DU-145 cells also were probed with specific oligonucleotide probes for exons 6, 7, and 8. PCR fragments were cloned and sequenced to verify the nature of the alternative products. Sequencing was performed using an automated sequencer (A.L.F., Pharmacia) using both T7 Sequenase and cycle sequencing. To quantitate the

different levels of expression of SHBG mRNA from the epi and fib cells, two additional PCR reactions were done to determine levels of two control mRNAs, b-2 microglobulin and PBGD.

Two major PCR products were amplified in all of the prostate samples, one at  $\approx 500$  bp and another at  $\approx 300$  bp. Prostate fib cells appeared to express 3 to 5 fold greater levels of both forms of SHBG than did epi cells. The  $\approx 500$  bp band was detected with all of the exon specific probes, while the  $\approx 300$  bp band did not bind exon probe 7, indicating that this region was missing from the  $\approx 300$  bp band. DNA sequencing confirmed the composition of this small band. Consistent with the alternative processing of androgen binding protein, and our observations of SHBG alternate transcripts in breast, exon 7 and a single base at the beginning of exon 8 were missing in the  $\approx 300$  bp band. The base deletion at the beginning of exon 8 could result in a frame shift and a new stop codon. An mRNA incorporating the loss of exon 7 and frame shift in exon 8 would result in protein without steroid binding activity.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/048		<b>Status:</b> Terminated	
<b>Title:</b> Localization and Identification of Sex Hormone Binding Globulin (SHBG) mRNA and SHBG Related Proteins in Breast Cancer (Production of Monoclonal Antibodies Using Mice)					
<b>Start Date:</b> 12/06/93			<b>Est. Completion Date:</b> Sep 97		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Katherine H. Moore, Ph.D.					
<b>Associate Investigators:</b> MAJ Richard R. Gomez, MC			MAJ Kenneth A. Bertram, MC		
<b>Key Words:</b> Cancer: breast, SHBG, mRNA,Animal Study					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		05/26/95	

**Study Objective:** The goal of this study is to further examine paraffin embedded breast tumor tissue for the expression of SHBG mRNA and to determine if breast cancer cells are producing alternate transcripts of SHBG, and begin characterizing those transcripts.

**Technical Approach:** The relatively new technique of polymerase chain reaction (PCR) *in-situ* hybridization will be modified for the study of breast tissue sections attached to glass slides. This technique will allow the determination of the association between cells expressing SHBG and tumor cells.

We will construct a cDNA library from ZR-75-1 mRNA, and sequence the clones containing SHBG and related inserts. Peptides will be synthesized based on the predicted amino acid sequence of the SHBG clones, and monoclonal antibodies produced. These monoclonal antibodies will be used for immunoprecipitation to determine if the alternate transcripts of SHBG in breast cancer cells are producing protein.

**Progress :** This protocol has been terminated and will be replaced by a revised version.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 92/058		<b>Status:</b> Completed	
<b>Title:</b> Is Sex Hormone Binding Globulin Locally Produced in Breast Cancer Tissue?					
<b>Start Date:</b> 05/01/92			<b>Est. Completion Date:</b> Jun 94		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Katherine H. Moore, Ph.D.					
<b>Associate Investigators:</b> Louis A. Matej, B.S.			MAJ Kenneth A. Bertram, MC		
<b>Key Words:</b> SHBG, breast cancer					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		//	

**Study Objective:** To gain insight into the regulation of breast cancer growth and development and to correlate the estrogen and progesterone receptor status of breast cancer biopsy tissue with the presence of sex hormone binding globulin (SHBG) mRNA.

**Technical Approach:** SHBG is a high affinity binding protein for androgens and estrogens. This protein is normally produced in the liver, released into the blood and functions to regulate the amount of free androgen or estrogen available for action at target organs. Recently, receptors for SHBG have been identified on prostate carcinoma cells. Prostate cancer, like breast cancer, is generally considered to be modulated by steroids. One proposed consequence of the SHBG receptor on cancer cells is the additional targeting of steroid to the cells. SHBG may have a role independent of steroid action and may be a growth factor itself. One of the oncogenes that is important in breast cancer development is p53. It has been found recently that changes in p53 and SHBG may be linked. Both of these genes are on the short arm of chromosome 17 near an area prone to rearrangement and mutation. Breast cancer cell lines (MCF-7 and ZR75-1, initially) will be examined for the presence of SHBG and mRNA and for factors that regulate transcription. In addition, the investigators will probe for SHBG mRNA in primary breast cancer tissue obtained at biopsy and surgery. Cancer cell membranes and primary tissue will be assayed for the presence of SHBG receptors. Techniques used will include Northern analysis, RIA of the conditioned media for expressed SHBG, and western analysis to determine the form of p53 expressed in the cells (wild type vs mutant). This study will thus characterize a potentially new oncogene for breast cancer and lead to a greater understanding of the mechanisms of cancer formation.

**Progress :** The goal of this study was to determine if SHBG was expressed in breast cancer cell lines and tumor tissue. Two indications of expression were used, mRNA detection by PCR, and protein detection using immunoprecipitation. Three breast cancer cell lines were employed, two estrogen receptor positive (MCR-7, ZR-75) and one ER negative (MDA-MB-231) Also, RNA was extracted from human breast samples collected from the pathology department. SHBG mRNA was detected in the three cell lines, as well as in 11 of 30 tissue samples. The presence or absence of a functional estrogen or progesterone receptor was not associated with the expression of SHBG. Also, we have found evidence of alternative splicing of the SHBG mRNA through DNA sequencing of the PCR product. It is unknown what function as alternative SHBG protein may have in breast cancer.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/041		<b>Status:</b> Completed	
<b>Title:</b> An in-vitro Biological Assay for Luteinizing Hormone Using the Testosterone Response of Isolated Leydig Cells From the Laboratory Mouse (Mus musculus) - Supplement Protocol to MAMC #91039 & #92092					
<b>Start Date:</b> 01/23/95			<b>Est. Completion Date:</b> Feb 96		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Katherine H. Moore, Ph.D.					
<b>Associate Investigators:</b> MAJ Robert M. Tuttle, MC			COL Dan C. Moore, MC		
<b>Key Words:</b> Luteinizing hormone, testosterone, Leydig cells, Mus musculus, Animal Study					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		//	

**Study Objectives:** This proposal is an addendum to existing protocols, MAMC #91039 and MAMC #92092. The objective of this study addendum is to perform the Luteinizing Hormone (LH) *in vitro* biological assay, which is employed in both protocols, using mouse leydig cells.

**Technical Approach:** Luteinizing hormone (LH) is a hormone produced in the pituitary gland with a primary site of action on the ovaries. Common methods used to measure levels of LH in blood samples include radioimmunoassay (RIA), membrane binding assays, and *in vitro* biological assays. The best measure of the biological activity of LH is the *in vitro* assay in which the normal cell response of steroid hormone production is used as a measure of hormone activity. The cells necessary for the estimated 200 assays (1600 tests for both protocols) will be derived from a total of 44 Balb/C mice. A testosterone curve will be developed and used to determine the testosterone concentrations in the samples.

**Progress :** A reliable assay for the determination of levels of biologically active luteinizing hormone in human blood samples was established. Earlier attempts to use a leydig cell tumor cell line to determine LH biological activity was not successful. Repeatable results and the required sensitivity could not be achieved in our laboratory. The successful assay used leydig cells isolated from mice on the day of the assay. The cell's response to LH in the sample was reflected in the amount of testosterone released by the cells in short term (2 hr) culture. The testosterone levels in the conditioned culture media were detected by RIA.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/143	<b>Status:</b> On-going
<b>Title:</b> Adolescent Risk Behavior and the Influence of Parents and Education		
<b>Start Date:</b> 09/02/94	<b>Est. Completion Date:</b>	
<b>Department:</b> Clinical Investigation	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> Troy H. Patience, B.S.		
<b>Associate Investigators:</b> MAJ Brent V. Nelson, MC		
<b>Key Words:</b> risk behavior:adolescents, parents, education		
<b>Accumulative</b> <b>MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative</b> <b>OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** 1. To determine the level of involvement of a sampling of 7th grade students in alcohol use, illegal drug use, sexual activity, and gang participation. 2. Assess student and parent general knowledge concerning alcohol use, illegal drug use, sexual activity, and gang participation. 3. Survey parental involvement in providing students with information and guidance. 4. Compare individual student's report of interaction with parents concerning the above topics, with their parent's report of interaction. 5. Determine if parent's level of general knowledge concerning alcohol use, illegal drug use, sexual activity, and gang activities, and parental involvement in providing students with information and guidance, have any effect on adolescent risk taking behavior.

**Technical Approach:** Approximately 1000 7th grade students and their parents will be surveyed in this study. Each student will be given a packet that includes a student survey, numbered student response sheet, parent survey, numbered parent response sheet with a number corresponding to the student response sheet, stamped envelope with MAMC address, stamped envelope with no address. Parents will complete their survey, place it in the unaddressed envelope and the student will place that envelope and their own response sheet in the addressed envelope. This will insure the student and the parent surveys are paired while still maintaining anonymity.

Survey results will be entered into a database for calculation of responses. Chi-square distribution will be used to compare parent and student paired responses, with statistical significance accepted at  $p \leq 0.05$ . General knowledge questions will be tabulated for parent and student in a percentage correct format.

**Progress :** 209 students in 2 schools have been surveyed those far, 94 parents returned surveys. This study is still planning to enroll 1000 students plus their parents. Due to several problems (i.e. school district resistance and slow school district approval) only 2 schools were surveyed. In addition the original principal investigator moved to San Diego. It is our intention to survey more kids in the San Diego area, and if a family practice PI can be found at MAMC to do more surveys in Tacoma area schools. A paper was written for submission to the Steger award competition.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/014	<b>Status:</b> On-going
<b>Title:</b> Relationships Between A Female Soldier's Military Occupational Specialty (MOS) and Birth Outcomes		
<b>Start Date:</b> 11/04/94	<b>Est. Completion Date:</b> Jan 96	
<b>Department:</b> Clinical Investigation	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Richard A. Sherman, MS		
<b>Associate Investigators:</b> R.J. Palowski Noble	F.A. Creedon J. Aro R Johnson	
<b>Key Words:</b> Female soldiers:birth outcomes, MOS		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objectives:** The purpose of this investigation is to attempt to quantify risk utilizing Risk Ratio and Odds Ratio risk estimates and establish baseline rates for the offspring of female soldiers by Career Management Field (CMF) or MOS for the following outcomes: spontaneous abortions, ectopic pregnancies, intrauterine fetal demise, preterm birth, low birth weight infant, and as a mechanism to intervene in these adverse outcomes.

**Technical Approach:** A prospective cohort study will be performed at the following locations: Ft. Carson, Ft. Hood, Ft. Lewis, Ft. Bragg, Ft. Campbell, and Ft. Riley. Respondents will be enrolled during OB registration classes from 1 October 1994 through 31 January 1995 and then followed through September 1995 to allow the subjects to progress through their pregnancies and develop outcomes. All pregnant soldiers and pregnant wives and daughters of soldiers limited to those eligible for care. Demographic variables will be ascertained by way of a proctored questionnaire given to the mother at the time of the initial OB registration. Outcome data will be obtained through the use of a questionnaire located in the OB record, which will be compiled in the newborn nursery. The number of subjects required to provide sufficient power is estimated to be 5,000 composed of 1,670 soldiers and a comparison group of 3,330 spouses and daughters. The CMF/MOS's likely to meet these requirements are 91B and 92A. Soldier jobs could also be classified into the following categories for analysis: Medical Maintenance, Administrative, Logistics, Food Service, Law Enforcement, Communications, and Other.

**Progress :** 850 subjects have been entered. No further subjects are being entered at this time. Data from current subjects are being recorded as they deliver. All data will be combined with data from the other military sites at the end of the collection period.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/139		<b>Status:</b> On-going	
<b>Title:</b> Pilot Study for Wound Healing Using Pulsed Electromagnetic Field Therapy					
<b>Start Date:</b> 04/21/95			<b>Est. Completion Date:</b>		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Richard A. Sherman, MS					
<b>Associate Investigators:</b> LTC John B. Whittemore, AN			CPT Thomas K. Curry, MC		
<b>Key Words:</b> Pulsed Electromagnetic Field Therapy, wound healing					
<b>Accumulative</b> <b>MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative</b> <b>OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		//

**Study Objectives:** The overall objective is to determine whether pulsing electromagnetic fields (PEMFs) can potentiate post operative recovery by increasing the rate of incisional wound healing and decreasing pain management requirements in patients undergoing abdominal and vascular surgery whose wounds are left open for secondary closure. The objective of this particular study is to perform a pilot which will provide trained staff and practiced methodologies for a larger study.

**Technical Approach:** This project is designed as a pilot to test the objectives as described and to prepare personnel and methods for a larger study with more subjects. The study is designed as a semi-double blind, randomized, two-group experimental repeated measures design. Ten subjects will be randomly assigned to two groups of five each. One group will receive PEMF treatment and the other will receive placebo treatment. The study will be double-blinded for the PEMF technician as well as the evaluators. Subjects will be males or females, over 18 years of age, who have undergone abdominal or vascular surgery at MAMC and who have incisions healing by secondary intention. Patient information will be collected pertaining to pre-existing disorders that may act as confounding variables to normal wound healing. All eligible subjects will be sequentially entered into the study until the groups are full. Wound healing will be assessed by ASEPSIS (a wound healing and infection assessment), videothermography, photography, and plenography (a computer program used to trace and compare wound outlines). Post operative incisional pain will be assessed by a Visual Analog Scale and post-operative analgesic usage. Each variable will be initially analyzed separately. The non-parametric variables will be analyzed using a two-way, repeated measures, non-parametric analysis of variance. The parametric variables will be analyzed with a parametric repeated measures ANOVA.

**Progress :** Two patients have been entered into the pilot study. Patient accrual continues.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/127		<b>Status:</b> Completed	
<b>Title:</b> Biofeed back for Pain[colon] A Multipractitioner Outcome Study					
<b>Start Date:</b> 05/06/94			<b>Est. Completion Date:</b> Jun 96		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Richard A. Sherman, MS					
<b>Associate Investigators:</b>			Antje F. W. Goeken, Psy.D.		
<b>Key Words:</b> pain:biofeedback, low back pain, orofacial pain					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		//	

**Study Objective:** 1) To determine the short term effectiveness of biofeedback interventions for chronic musculoskeletal low back pain and muscle related orofacial pain through a multipractitioner outcome study.;2) To test the proposed design, data gathering techniques, and scientist-practitioner interactions.

**Technical Approach:** Licensed clinicians who are members of the AAPB and meet its practice criteria will sequentially enter all patients who meet the diagnostic and other entrance requirements. The providers will fill out one form which details their usual treatment for the disorder. Very careful diagnostic categorization for each patient according to specified, standard criteria will be required. After treatment, each practitioner will send a form for each patient indicating deviations of the individual subject's treatment from their usual practice, number of sessions, objective outcome measures, and details of how the diagnosis was made. Each patient will keep a home log of pain and other factors for two weeks during the pre-treatment evaluation period, at the end of treatment, three-month after treatment, and six months after treatment. The patients will send their logs directly to the investigators. One thousand subjects with each disorder will be enrolled.

**Progress :** This study failed entirely as no patients actually completed participation. 61 practitioners agreed to begin the study. After confirmatory phone contacts, each practitioner received an explanatory tape and data packets to fill out or give to patients to fill out. Of these 61, 17 practitioners actually entered patients but no patients completed the study. A follow-up survey of practitioners indicated that it was just too much trouble to do the work involved in participation for free.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/153		<b>Status:</b> On-going	
<b>Title:</b> Use of Pulsing Electromagnetic Fields to Potentiate Healing of Stable, Open Ulcers on the Lower Limbs and Feet					
<b>Start Date:</b> 06/16/95			<b>Est. Completion Date:</b> Dec 97		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Richard A. Sherman, MS					
<b>Associate Investigators:</b> MAJ Arnoldas S. Kungys, MC Melissa Wong, BA			LTC Delbert E. Casey Jones, MC Estelle Hamblen, BA, MHA		
<b>Key Words:</b> pulsing electromagnetic field, ulcers, feet, lower limbs					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> //

**Study Objective:** To determine whether pulsing electromagnetic fields (PEMFs) can potentiate healing of stable, open ulcers on the lower limbs when used simultaneously with standard treatments relative to the rate of healing with placebo PEMF and standard treatment.

**Technical Approach:** Skin ulcers on the feet and legs are a highly significant clinical problem for patients with compromised neurovascular systems such as diabetics. We will perform a double blind study in which subjects will be randomly assigned to placebo PEMF and standard treatment or real PEMF and standard treatment. The patients will be those with diagnosed metabolic abnormalities (almost all will be diabetic) and have skin ulcers on their feet and lower legs which have not healed during the previous three months. Patients will be stratified by grade (I/I, III, and IV), location and diameter (< 1cm, 2.01 to 3.0 cm and >3.0 cm) of the ulcer as well as age and then randomly placed in either a placebo or real PEMF group. PEMF therapy (or placebo PEMF) therapy) will be performed five days per week for one hour per day until the ulcer heals or six weeks. Rate of ulcer healing will be measured by photographing the ulcer on the first day of treatment and once every seven days for the duration of participation. A special high resolution, set distance, light controlled camera in conjunction with a plenometer to measure the cross-sectional area of the ulcer as recorded on the photographs will be used. Videothermograms will be taken nearly simultaneously with the light photographs from a standard distance using standard settings to evaluate changes in near-surface blood flow (very highly correlated with healing rate). A power analysis of previous results shows that 3 subjects will be needed in each group assuming (a) that we predict the PEMF group will do better (one-tailed test) and (b) an 80% chance of finding a difference between the two groups at a 0.05 level of significance. A total of about 80 subjects will be started to account for dropouts. The data will be analyzed using a repeated measures analysis of variance.

**Progress :** No subjects have been entered, awaiting the completion of clinical patients before starting protocol.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/019		<b>Status:</b> On-going	
<b>Title:</b> Development/Infection Resistant External Fixater Sys & A Tibially Implanted, Percutaneous Limb Prosthetic Holder/Overlapping Ph III & IV[colon] Tests of Resistance to Infection & Skin Ingrowth In a Goat Model					
<b>Start Date:</b> 11/18/94			<b>Est. Completion Date:</b> Dec 97		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Richard A. Sherman, MS					
<b>Associate Investigators:</b> E.J. Lisecki			LTC Delbert E. Casey Jones, MC S. Cook		
<b>Key Words:</b> external fixater,limb prosthesis:tibia,Animal Study,goat					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		//

**Study Objectives:** The overall objectives for this program are to (a) develop a prosthetic attachment system for amputees which can be directly implanted into the major weight bearing bone and be extended through the skin (percutaneously) and (b) develop an external fixater pin coating which will resist infection for at least one year. Specific objectives of this study are to determine whether goats will develop infections when hydroxyapatite (HA) coated or uncoated screws are implanted into bone through the skin and left in place for eight months. HA is a substance normally found in bones which is used to coat artificial hips and knees in order to get bone to grow into the prostheses. The other specific objective is to determine whether a percutaneously implanted prosthetic will function under normal patterns of weight and movement without infections, loosening or other problems for at least one year.

**Technical Approach:** This study will utilize a total of 14 goats to test the objectives stated above. For the first specific objective, HA coated and uncoated screws will be percutaneously placed into the radius of ten goats with the shanks of the screws protruding 1/2 to 3/4 inch through the skin. The screws will be left in place 8 months. Biweekly blood work and daily observations of the site along with daily observation of the goats behavior and gait will insure that infections are diagnosed and treated immediately. After eight months, the screws will be removed and signs of chronic infection and tracts along the shanks will be noted. For the second specific objective, four goats will have HA coated, prosthetic limbs implanted after amputation of the left front leg below the goat's wrist. The goats will be monitored daily for discomfort and infection and intervention will be made as necessary. The animals will be maintained for as much of their natural lives as funding will afford for continued observation.

**Progress :** Protocol is on hold pending funding.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/020		<b>Status:</b> On-going	
<b>Title:</b> Development of an Infection Resistant External Fixater					
<b>Start Date:</b> 11/18/94			<b>Est. Completion Date:</b> Dec 97		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Richard A. Sherman, MS					
<b>Associate Investigators:</b> E.J. Lisecki			LTC Delbert E. Casey Jones, MC S. Cook		
<b>Key Words:</b> External fixaters,hydroxyapatite					
<b>Accumulative</b> <b>MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative</b> <b>OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> //

Study Objectives: To determine whether patients having standard fixaters coated with Hydroxyapatite (HA) will have significantly fewer infections than those having the same external fixaters not coated with HA.

Technical Approach: The proposed protocol is intended to solve the infection problem with external fixaters and work toward developing a percutaneously implanted prosthetic holder which would eliminate most of the reasons lower limb amputees are debilitated. This protocol is approved at Fitzsimmons Army Medical Center (FAMC). It was originally approved as protocol 90/208A in 1990 and has been re-approved since by both the human and animal use committee. It now carries the designation 94/208A with FAMC's animal use committee. We plan to perform the human use and goat transcutaneous rod portions of the study at Madigan. The goat prosthetic holder would be mounted on goats at FAMC. The goats would be transported to Madigan for long term holding after they stabilize. The human portion of the proposed study will not begin until the goat transcutaneous rod portion has been completed and the FDA has approved implanting HA coated external fixaters into humans for purposes of the study. Considerable detail about the animal portions of the study are presented in this protocol to support the proposed human work. This protocol will not be performed without outside funding.

Progress : Protocol is on hold pending funding.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/010		<b>Status:</b> On-going	
<b>Title:</b> Evaluation of the Performance Impact and Treatment of Exercise Induced Urinary Incontinence Among Female Soldiers					
<b>Start Date:</b> 11/04/94			<b>Est. Completion Date:</b> Apr 96		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Richard A. Sherman, MS					
<b>Associate Investigators:</b>			LTC Richard A. Sherman, MS		
<b>Key Words:</b> female soldiers:incontinence, exercise, performance impact					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//	

**Study Objective:** 1) To determine the incidence of exercise induced urinary incontinence among female soldiers, 2) the impact of urinary incontinence upon female soldiers' ability to perform their exercises and tasks, 3) the effectiveness of standard treatments for exercise induced stress and urge urinary incontinence, and 4) the effectiveness of urinary tract biofeedback and exercise training for stress and urge urinary incontinence.

**Technical Approach:** Study participants will perform a simulated PT test after drinking 500 ml (1 pint) of an electrolyte balanced fluid. A pre-weighed absorbent pad will be worn and then placed in a plastic bag following completion of the PT test for weighing to determine how much urine was lost. Tests will be conducted to determine a diagnosis of stress incontinence or motor/urge incontinence.

Patients will be randomized to one of two groups. Group 1 will do Kegel Exercises twice a day (10 minutes each session) for four weeks. Group 2 will do Kegel Exercises twice a day (10 minutes each session) for four weeks plus biofeedback training (30 minute treatments three times per week). Both groups will also receive a 20 minute tape recorded exercise to use twice per day, which will help recognize when the muscles are tenser than they should be.

Following the four weeks, patients will be reevaluated to determine if surgery is still necessary for stress incontinent patients or medication for motor/urge incontinent patients. Patients going on to surgery or medication will be reevaluated after recovery and stabilization of the problem. These tests will be repeated again approximately six months later.

**Progress :** 254 subjects have been entered. 82 of the 254 subjects have reported significant amounts of urinary incontinence during exercise and field training. Subject accrual continues.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/158	<b>Status:</b> On-going
<b>Title:</b> Pilot Study For[colon] Environmental-Temporal Relationships Between Changes in (a) Paraspinal Muscle Tension and Low Back Pain and (b) Trapezius Muscle Tension and Migraine and Tension Headache Intensity		
<b>Start Date:</b> 06/16/95	<b>Est. Completion Date:</b> Feb 97	
<b>Department:</b> Clinical Investigation	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Richard A. Sherman, MS		
<b>Associate Investigators:</b>		
C. Hill	Melissa Wong, BA	
Estelle Hamblen, BA, MHA	Linda Robson, BA	
Antje F. W. Goeken, Psy.D.	Kimberly A. Hermann-Do, BS, MHA	
<b>Key Words:</b> muscle tension:paraspinal, muscle tension:trapezius, migraine, low back pain		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objective:** 1) To determine whether there is a temporal relationship between changes in paraspinal muscle tension and changes in musculoskeletal low back pain in patients' normal environments. 2) To determine whether there is a temporal relationship between changes in trapezius muscle tension and changes in intensity of migraine and tension headaches in patients' normal environments. 3) To determine whether environmental - temporal relationships between (a) musculoskeletal low back pain and paraspinal muscle tension pain and (b) trapezius muscle tension and migraine and tension headache change after successful biofeedback therapy.

**Technical Approach:** There will be ten subjects in each group with the groups consisting of patients diagnosed as having tension headaches, musculoskeletal low back pain, migraine headaches, or mixed migraine-tension headaches ( a total of 40 patients). Ten subjects per group are likely to be needed to detect consistent temporal relationships between pain and muscle tension reliably because the previous data were highly variable and idiosyncratic. Assignment to groups will be by diagnosis only as there are no controls, etc. The subjects will all be patients referred from the TMC's at Ft. Lewis or the Neurology and Family Practice clinics at Madigan AMC who meet the diagnostic criteria for entrance into the study. They will be between 18 and 55 years of age, be otherwise healthy, and of either sex. Each subject will have four consecutive days of ambulatory recordings during all waking hours before and after standard muscle tension awareness and control treatment which will take approximately six weeks. Headache patients will have their bilateral trapezius muscled tension recorded while low back pain patients will have their paraspinal muscles recorded. The motion sensor will be placed in the center of the back between the shoulder blades for all patients. The recorded will beep every hour to remind the subjects to record their pain levels and type of activity being engaged in. the beeper does not stop until a pain rating is entered on the keyboard. The intervention/treatment is not experimental and will be performed (and its success rated ) according the Surgical Research Service SOPs.

**Progress :** 7 subjects have been entered. The reliability portion of the study has been completed. Two subjects have begun the full study. Patient accrual continues.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 92/074		<b>Status:</b> Terminated	
<b>Title:</b> Microbiological Analysis of Male NGU Specimens by Polymerase Chain Reaction[colon] A Retrospective Study					
<b>Start Date:</b> 06/05/92			<b>Est. Completion Date:</b> Aug 92		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Robert S. Stewart, MS					
<b>Associate Investigators:</b>			MAJ Margot R. Krauss, MC		
<b>Key Words:</b> urethritis, polymerase chain reaction					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		//

**Study Objective:** To perfect new PCR assays and to determine the prevalence rates by PCR in male NGU samples collected February through April 1989 for human papillomavirus (HPV), herpes simplex virus (HSV), human immunodeficiency virus (HIV), Chlamydia trachomatis, Trichomonas vaginalis, and Mycoplasma genitalium and to compare prevalence rates from both culture and PCR methods for Chlamydia trachomatis.

**Technical Approach:** Approximately 200 male NGU urethral specimens were collected during the months of February through April 1989 for MAMC Protocol #89/19 "Urinalysis As A Screening Exam for NGU in Males Attending an STD Clinic." These samples were cultured for Chlamydia trachomatis and Urea plasma urealyticum and the remaining fraction was stored frozen at -20 degrees Centigrade. These stored samples will be thawed, processed for DNA extraction, and analyzed by PCR for organisms not previously suspected, including HPV, HSV, HIV, C. trachomatis, T. vaginalis, and M. genitalium.

**Progress :** PI has retired, left protocol suspended so new staff member could take over, however, no one had time or interest to do the study.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 92/073		<b>Status:</b> Terminated	
<b>Title:</b> Molecular Microbiology Assay Development					
<b>Start Date:</b> 06/05/92			<b>Est. Completion Date:</b> Indef.		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Robert S. Stewart, MS					
<b>Associate Investigators:</b>			M. J. Styner, B.S.		
<b>Key Words:</b> molecular microbiology assay					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//	

**Study Objective:** To develop and improve assays required for other new and ongoing protocols.

**Technical Approach:** The scientific literature will be searched continually for reports of new assays, techniques, and methods dealing with molecular biology as it applies to microbiological diagnostics. These improved techniques will be tested in the lab at the Department of Clinical Investigation and assays developed as needed for application in other protocols. These assays will be evaluated with cultured organisms and discarded medical samples and tissues to insure that the methods developed have clinical value and function properly with both controls and clinical materials.

**Progress :** PI has retired, left protocol suspended so new staff member could take over, however, no one had time or interest to do the study.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/166		<b>Status:</b> Terminated	
<b>Title:</b> Effects of Gravity and Microgravity on Growth and Differentiation in Mus musculus Long Term Bone Marrow Culture					
<b>Start Date:</b> 09/21/94			<b>Est. Completion Date:</b>		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Mary C. Tillotson-Criss, BS					
<b>Associate Investigators:</b> D.J. Davis			M.B. Lilly CPT Rodger K. Martin, MS		
<b>Key Words:</b> bone marrow, Mus musculus, growth, gravity, microgravity, Animal Study, mouse					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		//	

**Study Objective:** To assess (1) the effects of microgravity on growth and differentiation of bone marrow cells; (2) to determine if bone marrow cells will grow in stimulated microgravity using collagen microspheres as a substrate; (3) to study the 3-D architecture of bone marrow to assist in determining tissue ultra-structure; (4) to develop and test normal murine bone marrow through infusion of in vitro grown cell culture marrow into syngenic mice in vivo.

**Technical Approach:** The mouse will be euthanized and both femurs removed to obtain bone marrow. The marrow will be placed into supplemented nutrient media, manual cell counts performed, and then placed into tissue culture flasks. Bone marrow cells will be grown in two different environments: gravity and simulated microgravity. Gravity's environment will be represented by using a tissue culture flask containing marrow cells, nutrient media, and special collagen beads that assist in cell adherence, then placed in an undisturbed horizontal position in 5% CO<sub>2</sub> incubator. Microgravity will be represented by using a tissue culture vessel containing equal amounts of marrow cells, nutrient media, and collagen beads. This vessel will continuously rotate about a horizontal axis. After obtaining optimal growing conditions for bone marrow cells by measuring glucose, CO<sub>2</sub>, O<sub>2</sub>, and pH levels, cell types will be determined by using special antibodies and stains. The investigator will be looking for these cells to change from immature to mature forms and will use antibodies to recognize surface antigen markers which are expressed as these cells mature (differentiate). In the microgravity environment it is anticipated that cells will have attached to the small collagen beads and developed so that a 3-D structure results. The investigator will examine the beads with an electron microscope in order to visualize cellular structure and their relationship to each other. To demonstrate functioning cells, male murine marrow cells grown from the two environments (gravity and microgravity) will be infused into immunologically compatible female mice which have had their bone marrow removed by irradiation. The mice will be observed daily for signs of becoming ill and then by the 30th day if the mice have survived the infusion and appear to be doing well, they will be euthanized and bone marrow from their femurs will be collected and examined for the presence of male hematopoietic cells.

**Progress :** Study was not begun since study was not funded by NASA.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF DENTISTRY**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/080	<b>Status:</b> Completed
<b>Title:</b> The Effect of Neuromuscular Blockade on Centric Jaw Relation		
<b>Start Date:</b> 03/17/95	<b>Est. Completion Date:</b> Mar 95	
<b>Department:</b> Dentistry	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Frank E. Orr, DC		
<b>Associate Investigators:</b>		COL Joseph C. Mulrean, DC
<b>Key Words:</b> Jaw, neuromuscular blockade		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objective:** 1) To demonstrate the effect of neuromuscular blockade has on centric jaw relation. 2) To demonstrate the influence dental malocclusion has on recording centric jaw relation.

**Technical Approach:** Thirty patients scheduled to undergo oral and maxillofacial surgical procedures with nasotracheal intubation will have their preoperative and intraoperative mandibular position measured in the horizontal plane. These measurements will be compared to determine what changes in jaw position occur with paralysis. The dental occlusion will be documented for each patient to determine if dental malocclusion contributes to significant differences in the preoperative and intraoperative measurements. The preoperative centric jaw relation record will be obtained using the bilateral manipulation technique with the patient in the reclined position by either the principle or associate investigator. Previously obtained models will then be mounted on a semi-adjustable articulator using an arbitrary facebow transfer. The anterior-posterior position of the mandibular cast will be measured at three points (most anterior tooth and bilaterally at the second molars) with a Erickson Model Platform Measuring Device and recorded to an accuracy of 0.1 mm. General anesthesia will be induced and the patient will be paralyzed with a nondepolarizing muscle relaxant. The loss of the Train of Four with a peripheral nerve stimulator will verify neuromuscular blockade. The patient will then be nasally intubated for the planned procedure. The intraoperative centric jaw relation record will be taken in the same fashion as the preoperative record using rapid set bite registration material. The mandibular model will then be remounted on the articulator using the new centric jaw relation record and measured at the same points. The patients will be categorized according to their classification of dental occlusion.

**Progress :** 30 subjects were entered. Manuscript has been written but not yet submitted for publication. The results of this study demonstrate that general anesthesia and neuromuscular blockade have minimal effect on the anteroposterior position of CR when recorded intraoperatively.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF EMERGENCY MEDICINE**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/120		<b>Status:</b> On-going	
<b>Title:</b> The Randomized Use of Helium-Oxygen Mixture for the Treatment of Acute Exacerbations of Chronic Obstructive Pulmonary Disease. A Blinded Trial					
<b>Start Date:</b> 06/09/93			<b>Est. Completion Date:</b> Dec 93		
<b>Department:</b> Emergency Medicine			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Richard D. Brantner, MC					
<b>Associate Investigators:</b> CPT David A. Della-Giustina, MC LTC Bernard J. Roth, MC			CPT James W. Thompson, MC CPT Timothy R. Murray, MC		
<b>Key Words:</b> COPD, helium,oxygen					
<b>Accumulative</b> <b>MEDCASE Cost:</b>		<b>Est. Accumulative</b> <b>OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$800.00		//	

**Study Objective:** To determine the therapeutic role of Heliox administration in the treatment of acute exacerbation of chronic obstructive pulmonary disease.

**Technical Approach:** Patients presenting with an acute exacerbation of COPD and requiring urgent treatment and agree to participate will be randomized to receive either Heliox (a mixture of 75% helium and 25% oxygen) or nitrogen-oxygen (a mixture of 75% nitrogen and 25% oxygen). Pulse oximetry will be monitored and any patient whose level falls to less than 90% will receive supplemental oxygen at a rate sufficient to raise pulse oximetry to at least 90%. Spirometry will be performed to measure FEV<sub>1</sub>, FVC, and PEF<sub>R</sub>. Base line arterial blood gas analysis will be performed and an upright portable chest x-ray will be obtained. Patients will be asked to score the severity of symptoms and the time to relief of those symptoms. All patients will receive nebulized albuterol treatments every thirty minutes for a total of 3 treatments. Patients will be re-evaluated after each treatment and at the end of the 90 minutes study period all patients will be placed on room air. Ten minutes after discontinuation of heliox or nitrogen-oxygen treatment, an arterial blood gas will be obtained, spirometry performed and the patients will be instructed not to discuss or divulge the mode of treatment they received. Patients will be evaluated at this time by a pulmonologist who will be blinded as to the treatment used. After evaluation of the patient, baseline and end of study data a determination will be made for 1) probable admission, 2) possible admission, 3) or admission not necessary.

Biographical data will be evaluated using the t test. The subjective rate of improvement in symptoms between the groups will be analyzed using the Mann-Whitney U Test and percentage improvement in FEV<sub>1</sub> will be compared using regression analysis.

**Progress :** 28 subjects were enrolled in FY 95, making the total number of subjects to date 48. An interim data analysis is scheduled once 50 subjects have been enrolled.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/116		<b>Status:</b> On-going	
<b>Title:</b> Multicenter, Prospective, Double-Blind Randomized Comparative Trial to Evaluate the Treatment Effects of Ciprofloxacin for 7 Days, Compared with Standard Therapy for 14 Days, In...acute Pyelonephritis					
<b>Start Date:</b> 06/03/94			<b>Est. Completion Date:</b> Jul 95		
<b>Department:</b> Emergency Medicine			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Thomas F. Burke, MC					
<b>Associate Investigators:</b> E.U. Etzkorn			LTC Ronald H. Cooper, MC MAJ Joseph T. Morris III, MC		
<b>Key Words:</b> pyelonephritis, ciprofloxacin					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		//	

**Study Objective:** To compare the treatment effects of ciprofloxacin (IV single dose/PO or PO) versus standard therapy (IV single dose/PO or PO) as outpatient management in premenopausal females with acute uncomplicated pyelonephritis. The efficacy and tolerability of a seven day treatment of ciprofloxacin will be compared with a fourteen day treatment with standard therapy. In addition, healthcare resource utilization will be evaluated related to treatment drop-outs, failures/relapses, as well as adverse events between both treatment arms (direct costs). Patient perception will be collected by recording patient's speed of recovery and return to normal activity.

**Technical Approach:** Premenopausal women with clinical signs and symptoms of acute pyelonephritis and pyuria are eligible to participate in this study. After enrollment, study drug (ciprofloxacin or Trimethoprim/Sulfamethoxazole) may be administered as an initial single IV. dose, or oral dose, followed by oral therapy for a total duration of therapy of 14 days of active study medication for the control arm, versus 7 days of active drug for the investigational arm, followed by 7 days of placebo. All patients enrolled in the trial (including failures and drop-outs) will be followed until 4-6 weeks following the completion of study drug. The primary outcome parameter will be bacteriological and clinical efficacy. A secondary parameter is the overall costs associated with pyelonephritis treatment of the two regimens. Patient perceptions will be collected by questioning the patient regarding their response to treatment.

**Progress :** Forty-three subjects have been enrolled in this study (36 in FY95). Two subjects were hospitalized, one with a kidney stone and the other for worsening pyelonephritis. No study-wide adverse events were reported.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/074	<b>Status:</b> On-going
<b>Title:</b> A Multi-center, Prospective Study of the Microbiology and Treatment of Infected Dog and Cat Bite Wounds		
<b>Start Date:</b> 03/04/94	<b>Est. Completion Date:</b> Jun 95	
<b>Department:</b> Emergency Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Thomas F. Burke, MC		
<b>Associate Investigators:</b> W. Evans		CPT Jack K. Handley, MC
<b>Key Words:</b> bite:cat, bite:dog;		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objective:** To describe the relative presence of various zoonotic and non-zoonotic pathogens in the microbiology of infected cat and dog bites.

**Technical Approach:** This is a multi-center study. Patients who have sustained a dog or cat bite would infection presenting for care more than 12 hours after being bitten will be invited to participate in this study. Volunteers will have one set of both aerobic and anaerobic wound culture(s) specimens to be sent to a reference lab. A complete blood count, blood cultures, and soft tissue and bone x-rays are not part of the study but are suggested when indicated. A history and physical examination will be performed upon study entry. Specifically noted in the history will be the type of and age of biting animal (dog or cat), the time of the wound, the time of onset of the wound infection and fever if present, and the presence of any immunocompromising conditions. Also noted will be any local wound care, the number and location of wounds, the presence and measured area of erythema, the presence of lymphangitis, the presence of swelling, the presence of purulent drainage, fluctuance and/or abscess formation. Any surgical procedures or debridements will be noted. The study endpoint will be the microbiological characterization of the pathogens associated with 100 dog and 50 cat bites. A tabulation of parenteral and/or oral antibiotic administered will be made. Recording of discontinuation or initial antibiotics because of clinical failure will also be made. Correlation of clinical failure and antibiotic susceptibilities will be analyzed.

**Progress :** Eighteen patients have been enrolled in this study. Collection of microbiologic specimens is planned to continue another ten months.

### Detail Summary Sheet

**Date:** 30 Sep 95                      **Protocol No.:** 94/135                      **Status:** On-going

**Title:** Multicenter, Randomized, Double-Blind, Parallel Trial, Comparing the Efficacy and Safety of a Single IV Dose (1.5 mg/kg) of Selfotel with Placebo in Patients Age 40-85 Years with Acute Ischemic Stroke

**Start Date:** 08/05/94                      **Est. Completion Date:**

**Department:** Emergency Medicine                      **Facility:** MAMC

**Principal Investigator:** CPT Thomas F. Burke, MC

<b>Associate Investigators:</b>	MAJ John W. McBurney, MC
MAJ Jonathon Newmark, MC	CPT Leo W. Kesting, MC
MAJ Ronald E. Schwartz, MC	MAJ William T. Hurley, MC
J.L. Hobbs	G.W. Beaver
M.M. Swansberg	J.N. Piper
CPT Eric I. Hassid, MC	C.L. Rodriquez

**Key Words:** stroke:ischemic, Selfotel, placebo

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	//

**Study Objective:** 1) To evaluate the efficacy and safety of a single 1.5 mg/kg dose of selfotel relative to placebo in improving the 90-day functional outcome of acute ischemic stroke patients. 2) To determine whether selfotel improves the 30-day and 90-day outcome compared with placebo. 3) To determine whether selfotel reduces mortality from acute ischemic stroke compared with placebo.

**Technical Approach:** There will be three periods to this trial: Screening/Treatment, Acute Monitoring, and Follow-up. Screening/Treatment Period: The Screening/Treatment period begins when the patient is admitted to the Emergency Room. This trial will enroll patients 40-85 years with a clinical diagnosis of parietic hemispheric acute ischemic stroke. Baseline neurologic symptoms will be documented with the Scandinavian stroke Scale and the National Institutes of Health (NIH) Stroke Scale. Screening procedures and treatment must be accomplished as soon as possible and no longer than six hours from the onset of the patient's stroke symptoms. Patients will be randomized to 1.5 mg/kg selfotel or placebo. A single dose of trial drug will be given. Acute Monitoring Period: The Acute Monitoring period begins immediately after trial drug administration and ends on Day 8 or hospital discharge (if earlier). During this acute period, the patients will be monitored for safety and neurologic function. Follow-up Period: The Follow-up period begins after Day 8 or when the patient is discharged from the hospital (if earlier). Clinic visits will be made on Trial Days 30 and 90 when efficacy will be determined using the Barthel Index, NIH and Scandinavian Stroke Scales.

**Progress :** No patients have been entered in this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/189	<b>Status:</b> On-going
<b>Title:</b> Analgesia for Reduction of Acute Glenohumeral Dislocation[colon] Intra-articular Lidocaine Versus Intravenous Fentanyl		
<b>Start Date:</b> 09/15/95	<b>Est. Completion Date:</b> Aug 96	
<b>Department:</b> Emergency Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> J. R. Hoffman		
<b>Associate Investigators:</b> M. Coppola		R. Butler V. Gennaro
<b>Key Words:</b> glenohumeral dislocation, lidocaine, Fentanyl		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

Study Objectives: We intend to contrast the analgesic efficacy of intra-articular lidocaine versus intravenous fentanyl in an adult population suffering from acute glenohumeral dislocation.

Technical Approach: A sample of 40 consenting patients (male and female) meeting diagnostic and inclusion criteria would be enrolled in the study. They would be randomized to receive either intravenous fentanyl or intra-articular lidocaine as analgesia for the reduction of their shoulder dislocation. Reduction would be performed by a standardized technique and their shoulder immobilized for post-reduction radiographs. Patients would be asked to rate their pain at presentation, pain at the administration of analgesia, pain of reduction, level of sedation, and pain at time of discharge on a visual analog scale. The clinician would also rate the ease of reduction. Data would undergo analysis of variance (ANOVA). The patient's score and the physician's score would be subjected to regression correlation.

Progress : Submission of revised 5303-R still required before protocol can start.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/152		<b>Status:</b> On-going
<b>Title:</b> Pediatric Intubation Training Utilizing the Ferret Model				
<b>Start Date:</b> 08/16/94		<b>Est. Completion Date:</b>		
<b>Department:</b> Emergency Medicine		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Steven A. Pace, MD				
<b>Associate Investigators:</b> MAJ Lawrence A. Wilson, MC		CPT Thomas F. Burke, MC		
<b>Key Words:</b> intubation:training, ferret,Animal Study				
<b>Accumulative</b> <b>MEDCASE Cost:</b>		<b>Est. Accumulative</b> <b>OMA Cost:</b>		<b>Periodic Review:</b>
\$0.00		\$0.00		//

**Study Objective:** To enhance the clinical skills of health care providers in managing pediatric airways, specifically endotracheal intubation.

**Technical Approach:** Ferrets will be anesthetized and course participants will be given the opportunity to intubate a ferret employing a laryngoscope and endotracheal tube. Administration and monitoring of anesthesia will be directly supervised or performed by the attending veterinarian. The veterinarian will be present at all times to assist, modify, or terminate the procedure.

**Progress :** Three training session were held in FY 95 with 4 animals used in each session.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/183		<b>Status:</b> On-going	
<b>Title:</b> A Double-Blind, Randomized, Placebo-Controlled, Multicenter, Parallel Group Study to Demonstrate the Efficacy and Safety of GG167 in the Prevention and/or Progression of Influenza A and B Viral ....					
<b>Start Date:</b> 09/15/95			<b>Est. Completion Date:</b> Mar 96		
<b>Department:</b> Emergency Medicine			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Steven A. Pace, MD					
<b>Associate Investigators:</b> S.W. Powell			MAJ William J. Frohna, MC CPT Nathan T. Rudman, MC		
<b>Key Words:</b> GG167, influenza, safety, efficacy					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> //

**Study Objectives:** To demonstrate the efficacy of GG167 given by the inhaled, intranasal, and inhaled plus intranasal routes, in the prevention and/or progression of symptomatic disease caused by influenza A and B viral infection. Also, to further assess the safety of GG167 given by the inhaled, intranasal, and inhaled plus intranasal routes.

**Technical Approach:** This will be a double-blind, randomized, placebo-controlled, multicenter, parallel-group study to be conducted at 100 centers worldwide. Approximately 840 patients will be randomized to receive study medication twice daily or four times daily for five days and will attend a post-treatment visit on Day 6 and a follow-up visit on Day 21. Efficacy evaluation will be based on the presence of symptomatic influenza, daily symptom and severity assessments recorded by the patient on a Diary Card, global assessment of symptoms and temperature. Safety will be evaluated by baseline and post-treatment routine blood analysis and follow-up (if indicated) and adverse event monitoring during the study period. The primary endpoint is the proportion of patients with laboratory confirmed influenza plus at least two clinically significant influenza symptoms of greater than mild severity. The primary population for analysis will be the Intent-to-Treat population that 15% placebo patients will have symptomatic influenza and assume a clinically relevant difference as a decrease to less than or equal to 5% of patients with symptomatic influenza for the GG167 treatment group. Primary significance tests will be performed on data from all centers worldwide.

**Progress :** Study is awaiting MEDCOM approval.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/005	<b>Status:</b> Completed
<b>Title:</b> A Double-Blind, Randomized, Placebo-Controlled Multicenter Study to Investigate the Efficacy and Safety of GG167 Therapy in the Prevention of Progression of Influenza A and B Viral Infections		
<b>Start Date:</b> 10/21/94	<b>Est. Completion Date:</b> Jul 95	
<b>Department:</b> Emergency Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> Steven A. Pace, MD		
<b>Associate Investigators:</b> W.S. Powell R.B. Schwartz Gretchen Carrougher, RN		
MAJ William J. Frohna, MC A.R. Vacarro CPT Nathan T. Rudman, MC		
<b>Key Words:</b> GG167, influenza, prevention		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** 1) To evaluate the efficacy of GG167 in the prevention of progression of influenza A and B viral infections (asymptomatic to symptomatic), 2) to evaluate the safety of GG167 in the prevention of progression of influenza A and B viral infections (asymptomatic to symptomatic), and 3) to determine route(s) of administration for Phase III protocol design.

**Technical Approach:** A medical history will be obtained and a physical examination performed including blood and urine tests and a nasal wash. Patients will be randomly assigned to one of the four treatment groups; 1) GG167 (16 mg/ml) two sprays per nostril twice a day and a dry powder placebo which will be inhaled twice a day through the mouth, 2) GG167 (5 mg) inhaled by mouth two times twice a day and placebo nasal spray two sprays per nostril twice a day, 3) GG167 dry powder inhaled two times a day plus GG167 nasal spray two sprays per nostril twice a day, or 4) placebo nasal spray two sprays per nostril twice a day and placebo dry powder inhaled two times a day. The amount of medication given is approximately 0.2 ml into each nostril. The dry powder for inhalation contains 5 mg GG167 in each inhalation. Patients will be given a diary card to complete each morning and evening of flu symptoms and temperatures for 21 days.

After 5 days of treatment patients will return to the clinic for a follow-up physical examination, a second blood and urine sample and nasal washing. After a further 14-19 days of treatment, patients will return to the clinic for a final check-up and a blood test to look for antibodies to influenza.

**Progress :** This study was completed by study sponser, with no patients entered at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/006	<b>Status:</b> Completed
<b>Title:</b> A Double-Blind, Randomized, Placebo-Controlled Multicenter Study to Investigate the Efficacy and Safety of Inhaled and Intranasal GG167 in the Treatment of Influenza A and B Viral Infections		
<b>Start Date:</b> 10/21/94	<b>Est. Completion Date:</b> Jul 94	
<b>Department:</b> Emergency Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> Steven A. Pace, MD		
<b>Associate Investigators:</b> W.S. Powell R.B. Schwartz Gretchen Carrougner, RN	MAJ William J. Frohna, MC A.R. Vaccaro CPT Nathan T. Rudman, MC	
<b>Key Words:</b> influenza:progression, GG167		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** 1) To evaluate the efficacy of inhaled GG167 and the combination of inhaled and intranasal GG167 in the treatment of symptomatic influenza A and B viral infections and 2) the safety of inhaled GG167 in the treatment of symptomatic influenza A and B viral infections.

**Technical Approach:** A medical history will be obtained and a physical examination performed including blood and urine tests and nasal wash. Patients will be randomly assigned to one of the three treatment groups; 1) GG167 (5 mg) inhaled two times twice a day plus two 0.1 ml sprays per nostril twice a day of a placebo, 2) GG167 inhaled two times twice a day plus GG167 two 0.1 ml sprays per nostril twice a day, 3) placebo inhaled twice a day plus a two placebo spray per nostril twice a day. The concentration of GG167 is 16 mg/ml and the powder for inhalation contains 5 mg GG167 in each inhalation. Patients will be given a diary card to complete each morning and evening of flu symptoms and temperatures for 21 days.

After 5 days of treatment patients will return to the clinic for a follow-up physical examination, a second blood and urine sample and nasal washing. After a further 14-19 days of treatment, patients will return to the clinic for a final check-up and a blood test to look for antibodies to influenza. A quality of life questionnaire will be completed before starting treatment, the day after finishing treatment and 14-19 days later.

**Progress :** This study was completed by study sponser, with 9 patients entered and 7 completed the study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/165	<b>Status:</b> On-going
<b>Title:</b> Emergency Surgical Procedures Laboratory Training Utilizing the Goat (Capra hircus)		
<b>Start Date:</b> 09/21/94	<b>Est. Completion Date:</b> Oct 97	
<b>Department:</b> Emergency Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> Steven A. Pace, MD		
<b>Associate Investigators:</b> MAJ Lawrence A. Wilson, MC		MAJ William J. Frohna, MC
<b>Key Words:</b> emergency surgical procedures: training, goat, Animal Study		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

Study Objective: The objectives of this training exercise are to teach physicians one safe method of performing six life-saving procedures for trauma patients.

Technical Approach: The procedures listed below will be performed under the supervision of a staff member and the veterinarian assigned to Clinical Investigation. All animals will be anesthetized and then will be sacrificed immediately after the procedures. The procedures consist of: 1) Chest tube insertion, 2) Cricothyroidotomy, 3) Pericardiocentesis, 4) Diagnostic peritoneal lavage, 5) Venous cutdown, 6) Thoracotomy.

Progress : One training session was held in FY 95 with 3 animals used in the session.



### Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 95/185

**Status:** On-going

**Title:** A Double-Blind, Randomized, Placebo-Controlled, Multicenter, Parallel Group Study to Investigate the Efficacy and Safety of GG167 Administered Twice and Four Times a Day for the Treatment of Inf

**Start Date:** 09/15/95

**Est. Completion Date:**

**Department:** Emergency Medicine

**Facility:** MAMC

**Principal Investigator:** Steven A. Pace, MD

**Associate Investigators:**  
MAJ William J. Frohna, MC

CPT Nathan T. Rudman, MC  
W.S. Powell

**Key Words:** GG167, influenza

**Accumulative**

**MEDCASE Cost:** \$0.00

**Est. Accumulative**

**OMA Cost:** \$0.00

**Periodic Review:**

//

**Study Objectives:** To evaluate the efficacy of GG167 given by the inhaled and intranasal routes in the treatment of influenza A and B viral infections. To compare the efficacy of GG167 administered four times a day to twice a day in the treatment of influenza A and B viral infections. To evaluate the safety of GG167.

**Technical Approach:** This will be a randomized, placebo-controlled, multi-center, parallel-group study which will be double-blind to active or placebo treatment but not to dosing schedule. Approximately 720 patients will be randomized to receive study medication twice daily or four times daily for five days or to placebo treatment groups for both schedules and will attend a Post-treatment visit on Day 6 and a follow-up visit on day 21. Males or females  $\geq 13$  years of age with a duration of influenza-like illness of  $\leq 48$  hours (this must include feverishness and at least two of the following: myalgia, headache, cough, sore throat) prior to receiving the first dose of study medication will be included. Efficacy measurements will include daily symptom assessments in a diary card, global assessment of symptoms, temperature, use of relief medications, incidence of secondary infections and use of anti-infective medications. Safety will be evaluated using laboratory analysis of blood and clinical adverse events inquiries. The primary endpoint is the time until alleviation of clinically significant symptoms of influenza within the qualified Intend-to-treat population of all patients randomized to treatment. Placebo groups will be combined for statistical analysis. Statistical tests for efficacy will be pairwise comparisons of GG167 qds and GG167 bd against placebo. Time to alleviation will be analyzed using an extended Mantell-Haezel test, stratified for center. Other parameters will be tested using analysis of variance, the Fischer's Exact Test, or other appropriate statistical method.

**Progress :** Study is awaiting MEDCOM approval.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/052		<b>Status:</b> Terminated	
<b>Title:</b> Comparison of the Esophageal-Tracheal Combitube and Endotracheal Intubation in the Prehospital Management of Cardiac Arrest					
<b>Start Date:</b> 02/04/94			<b>Est. Completion Date:</b> Jun 94		
<b>Department:</b> Emergency Medicine			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Tracey Shirk, MC					
<b>Associate Investigators:</b> MAJ Peter P. Taillac, MC			F. Fuller Marc McIlrath, R.E.M.T.-P.		
<b>Key Words:</b> combitube, cardiac arrest					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 01/20/95

Study Objective: To determine, using subjective and objective criteria, whether the Esophageal-Tracheal Combitube is an effective alternative to endotracheal intubation in the prehospital airway management of cardiac arrest patients.

Technical Approach: Patients in full cardiac arrest who are treated by EMS personnel will, on even numbered days, will be intubated with and endotracheal tube. On odd numbered days, the patient will be intubated with the Esophageal-Tracheal Combitube (ETC). The hypopharynx will first be visualized with a laryngoscope to insure no foreign body is present. An End-Tidal Carbon Dioxide Detection device will be used on all patients. Resuscitation will then proceed according to ACLS standards and Pierce County protocols until the patient is transferred to the receiving facility. If intubation attempts with either device fail, the patient may be intubated with the opposite device. Data from these intubation failures will be analyzed separately.

After transport to the receiving facility, EMS personnel and Emergency Department physicians will complete a data collection form on which they will describe their impressions of the effectiveness of airway management. They will comment on ease of intubation, adequacy of intubation, oxygenation, and ventilation, and any complications encountered. They will also document any available objective data (end-tidal CO<sub>2</sub> detection, pulse oximetry, and ABG results), and the patient outcome.

Data will be compiled and analyzed at frequent intervals by a physician medical monitor. If a statistically significant increase in complications or mortality rates is observed with ETC usage, the study will be immediately terminated. Data analysis will include chi-square for complication rates, subjective ease of use, and the number of attempts. Paired t-test will be used for arterial blood gas data.

Progress : PI could not overcome logistics of the civilian agents to collect the data and report it adequately and promptly.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF FAMILY PRACTICE**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/073		<b>Status:</b> Completed	
<b>Title:</b> Operational Medicine Curriculum for Army Family Practice Residency					
<b>Start Date:</b> 02/17/95			<b>Est. Completion Date:</b> Jul 95		
<b>Department:</b> Family Practice			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Donald M. Bradshaw, MC					
<b>Associate Investigators:</b> LTC William F. Miser, MC			Dr. Robert Collins		
<b>Key Words:</b> Curriculum, Family Practice Residency					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		//	

**Study Objective:** To develop a curriculum to teach Operational Medicine during the Army Family Practice Residency.

**Technical Approach:** This project has three parts: 1) to determine the non-clinical roles family physicians assume in their first assignment after graduation from residency. This will be done via a questionnaire to the 1992 and 1993 graduates from Army Family Practice Residencies. Descriptive and analytical analysis of the replies will be done. 2) Take these roles and using a modified Delphi technique with a panel of recognized experts, develop the topics to include in the curriculum. 3) Take these topics and describes teaching methods to include them in an Army Family Practice Residency.

**Progress :** 69 subjects were enrolled at MAMC. Manuscript submitted for Fellow's Award and to national journal. Finding include Army family physicians are given great responsibility early in their careers, assume different roles from other specialties, graduates do not feel well prepared for their non-clinical roles.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/151		<b>Status:</b> Completed	
<b>Title:</b> Factors Associated With Physician's Marriage Satisfaction					
<b>Start Date:</b> 09/02/94			<b>Est. Completion Date:</b>		
<b>Department:</b> Family Practice			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Kevin DeWeber, MC					
<b>Associate Investigators:</b>			MAJ David C. MacDonald, MC		
<b>Key Words:</b> marriage:physicians, satisfaction					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//	

**Study Objective:** To find those factors that are associated with high marital satisfaction among marriages comprised of at least one physician. This includes male and female physicians with a nonphysician spouse and dual physician marriages.

**Technical Approach:** Two questionnaires will be sent to both the husband and the wife. The first will be the Marital Assessment Questionnaire, a five item list that is a brief highly reliable assessment of marital satisfaction. The second is a 43 item questionnaire consisting of 9 demographic items and 34 items related to marriage and family life. Subjects dealt with include children, finances, medical practice, communication, and interpersonal relationships Regression analysis will be used to analyze the data.

**Progress :** 300 subjects entered. Study showed that the greatest predictor of higher marital satisfaction was intimacy - i.e. communication, sexual fulfillment, and meeting needs - and not medical related factors.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/047		<b>Status:</b> On-going	
<b>Title:</b> Healing of Sprained Ankles Using Pulsed Electromagnetic Field Therapy					
<b>Start Date:</b> 05/19/95			<b>Est. Completion Date:</b> Sep 95		
<b>Department:</b> Family Practice			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Richard T. Dombroski, MC					
<b>Associate Investigators:</b>			LTC Richard A. Sherman, MS		
MAJ James D. Terrio, MC			K. Willard		
MAJ Arnoldas S. Kungys, MC			Linda Robson, BA		
Estelle Hamblen, BA, MHA			Melissa Wong, BA		
<b>Key Words:</b> Pulsed Electromagnetic Field Therapy, ankle sprains					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//	

**Study Objectives:** To determine whether pulsing electromagnetic fields (PEMFs) can be useful in potentiating recovery from grade I and II sprained ankles when used in conjunction with standard techniques.

**Technical Approach:** This project is designed to confirm the results of an earlier, relatively small study performed by the Army. That study showed that soldiers exposed to PEMFs just after spraining their ankles recovered more quickly than those who were not exposed to them. This project is a multicenter study supported by Electropharmacology, INC. Approximately 40 subjects will participate at Madigan AMC and will have objective measures of recovery including range of motion (assessed by goniometry), pain assesement (by visual analog scale), level of activity, presence of swelling (by volumetric measure) and use of ice and medications. Soldiers between the ages of 18 and 50, diagnosed as having had either a Grade I or Grade II ankle sprain within 48 hours of evaluation will be ranndomly divided into (a) standard treatment plus active PEMF therapy or (b) standard treatment plus placebo PEMF therapy. Each patient's ankle will be placed under the device for 30 minutes for two consecutive days and swelling and pain will be assessed during a follow-up on day three. Changes in swelling will be analyzed using a non-paramentric two way repeated measures analysis of variance in which the repeated measure will be the subject's swelling at each evaluation and the independent measure will be the active vs. placebo group. Changes in pain, pressure, function, and differences in rate of initial swelling and then subsequent decrease, will be determined using a non-parametric correlation. Differences in amount of ambulation, range of motion and pain medication taken will be calculated using repeated measures analysis of variance and a slope analysis.

**Progress :** This project was delayed due to equipment problems which have all been resolved and patient enrollment has begun. 2 subjects have been entered at this time.

### Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 95/120

**Status:** Completed

**Title:** Alternative Health Care Usage Among Adult Patients in an Army Family Practice Clinic

**Start Date:** 03/17/95

**Est. Completion Date:** Dec 94

**Department:** Family Practice

**Facility:** MAMC

**Principal Investigator:** C. E. Drivdahl

**Associate Investigators:** None

**Key Words:** alternative health care, adults, family practice

**Accumulative**

**Est. Accumulative**

**Periodic Review:**

**MEDCASE Cost:** \$0.00

**OMA Cost:** \$0.00

//

**Study Objective:** To discover the percentage of adults enrolled in the MAMC Family Practice Clinic (FP) who use alternative health care, and define the demographics of these patients. To define or classify the type of alternative medical practices sought, and discover how the patient learned of this source. To discover what ailment or problem led the patient to seek out alternative medicine, and discover if the patient is using it in place of, or in conjunction with, traditional medicine. Discover if patients who use alternative medicine have shared this with their FP physician.

**Technical Approach:** This will be a descriptive study based on data collected from an anonymous survey which will be mailed to a randomly selected group of approximately 250 adults (based on pilot study of 25 patients, this should be enough to give statistically significant results), age 18-99 years, who are eligible to receive their health care in family practice. Patients will receive a letter asking them to complete the survey and return it as soon as possible. Each survey will be coded so that a second mailing can be sent to those who do not respond after approximately two weeks. The data will be tabulated to determine what percentage of the sample is using alternative medicine, determine if there is any significant differences in demographics between user and non-users, and determine the type of ailments that lead users to seek alternative medicine.

**Progress :** 250 questionnaires were mailed, with 176 being returned. 28% use alternative health care.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/177		<b>Status:</b> On-going	
<b>Title:</b> Comparison of Manipulative Treatment and Conservative Measures in the Management of Carpal Tunnel Syndrome (CTS)					
<b>Start Date:</b> 09/15/95			<b>Est. Completion Date:</b> Jun 96		
<b>Department:</b> Family Practice			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> B. R. Johnson					
<b>Associate Investigators:</b> D. Martin			COL Shashi J. Kumar, MC		
<b>Key Words:</b> Carpal tunnel syndrome, manipulation, home exercise program					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		//

**Study Objectives:** The objective of this study is to show that manipulation of the wrist and/or the thoracic outlet in combination with a home exercise program can alter the symptoms, function and/or nerve conduction latencies in carpal tunnel syndrome. It will be a prospective, randomized, controlled and partially blinded clinical trial.

**Technical Approach:** The subjects for the study will be consecutively drawn from a pool of patients referred to the Madigan Physical Medicine Department. All patients with suspected CTS will be given nerve conduction studies by the same physiatrist (S.K.). The patients with abnormal nerve conduction studies will be asked to enroll. All enrollees will be evaluated for level of function and mobility by an independent blinded investigator (D.M.) at the start and end of the study period. They will fill out questionnaires for demographic information, pain level, mobility and function. The individuals will be randomly assigned to the treatment or control group and will be blinded as to which group they are in. All subjects will be seen by the same physician (B.J.) weekly for the first month and every other week for the next two months for a total three month study period. At each visit, the control group will be asked to fill out pain scales and will be evaluated for range of motion. The treatment group will be asked to fill out pain scales and then treated using osteopathic methods (Sucher, 1993, 1995). The treatment group will also be instructed in a home exercise program. In addition to a final evaluation by D.M., each participant will be asked to fill out the questionnaires again and will be given repeat nerve conduction studies by the same physiatrist (S.K.) who will also be blinded.

We anticipate 40-50 subjects will be necessary to gain statistical significance, 20-25 in each of the groups. Analysis of the data will be done using nonparametric methods.

**Progress :** Protocol was just approved and has not started yet.



## Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 95/149

**Status:** On-going

**Title:** Primary Prevention of Otitis Media Using a Parental Education Model to Reduce Risk Factors

**Start Date:** 06/16/95

**Est. Completion Date:**

**Department:** Family Practice

**Facility:** MAMC

**Principal Investigator:** LCDR Robert C. Marshall, MC USNR

**Associate Investigators:**  
LT Joan Morris, NC USN

LT Mark Flynn, MC USNR

**Key Words:** Otitis media, education

**Accumulative**

**Est. Accumulative**

**Periodic Review:**

**MEDCASE Cost:** \$0.00

**OMA Cost:** \$0.00

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**Study Objectives:** The objective of this study is to reduce the incidence of acute otitis media by educating parents to modify known risk factors.

**Technical Approach:** All infants born at Naval Hospitals Bremerton and Oak Harbor for the month of April, May, June and July 1995 will be screened for exclusion criteria or Tri-care assignment to primary care portal outside of USNH Bremerton or Oak Harbor. If acceptable, the patient will be stratified and randomized to intervention and control groups. Each infant will be given a random number derived from a random number table. The control group will receive usual information on child care. In addition to this information, the intervention group will also receive a parental handout on risk factor modification of known behaviors that increase the risk of otitis media and a 10-15 minute talk by a nursery nurse or corpsperson about modifying these factors. All parents will complete a newborn risk factor questionnaire. At each well baby visit, ER visit and acute clinic visit, the child will be evaluated for otitis media using published criteria for diagnosis and a check-off sheet. Parents and infants in both groups will receive only routine care and counseling subsequent to the initial encounter. Follow-up questionnaires will be mailed at 6 and 12 months.

**Progress :** Sixty-four patients have been enrolled in this study at MAMC in FY95. 600 subjects projected by power analysis to detect 25% decrease in intervention group. Enrollment is expected to accelerate over the next several months.

### Detail Summary Sheet

**Date:** 30 Sep 95      **Protocol No.:** 93/013      **Status:** On-going

**Title:** Exercise Blood Pressure and Heart Rate Response in Pregnancy As A Predictor of Preeclampsia

**Start Date:** 11/06/92

**Est. Completion Date:**

**Department:** Family Practice

**Facility:** MAMC

**Principal Investigator:** CPT Craig M. Meier

**Associate Investigators:**

LTC Arthur S. Maslow, MC

MAJ Wade A. Lillegard, MC

CPT Janus D. Butcher, MC

CPT David N. Crouch, MC

LTC John P. Kugler, MC

CPT Monte C. Uyemura, MC

CPT Brain C. Harrington, MC

**Key Words:** preeclampsia, exercise, heart rate

**Accumulative**

**Est. Accumulative**

**Periodic Review:**

**MEDCASE Cost:** \$0.00

**OMA Cost:** \$0.00

09/21/94

**Study Objective:** To determine if blood pressure and heart rate response to exercise can be used to predict the development of preeclampsia in pregnant women.

**Technical Approach:** An estimated 200 obstetric patients seen at MAMC Departments of OB/GYN and Family Practice who are nulliparous and have no history of hypertension, diabetes, heart disease or thyroid disease prior to pregnancy will be enrolled. Stationary bicycle exercise stress test will be performed prior to 20 weeks gestation. Blood pressure and heart rate response to exercise, the independent variables, will be monitored and documented at prescribed intervals during the test. The dependent variable will be the development of preeclampsia, and will be recorded as categorical data.

**Progress :** 350 subjects have been enrolled in this study at MAMC. All subjects have completed exercise testing. Analysis is waiting for several more outcomes, as the last expected delivery date is 10 Jan 96.

### Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 94/053

**Status:** Terminated

**Title:** Does Treatment of Subclinical Hypothyroidism Improve Glycemic Control in Type II Diabetics

**Start Date:** 02/04/94

**Est. Completion Date:** Jun 94

**Department:** Family Practice

**Facility:** MAMC

**Principal Investigator:** CPT Jon K. Van Valkenberg, MC

**Associate Investigators:**  
MAJ Robert M. Tuttle, MC

M.L. Tuggy

**Key Words:** diabetes, obesity, levo-thyroxine

**Accumulative**

**Est. Accumulative**

**Periodic Review:**

**MEDCASE Cost:** \$0.00

**OMA Cost:** \$0.00

//

**Study Objective:** To determine if glycemic control can be improved by treating subclinical hypothyroidism in Type II diabetic patients.

**Technical Approach:** Fifty patients from the Endocrinology and Family Practice clinics with subclinical hypothyroidism and Type II diabetes will be identified. Patients may be on oral agents or insulin. These patients will have serum TSH values between 5 and 20 mIU/ml and have no clinical symptoms of hypothyroidism. The patients will be randomly assigned to one of two groups. The first group is the treatment group in which the TSH will be normalized with levothyroxine. Patients randomized to the second group will serve as the control or observation patients (no attempt will be made to normalize their TSH). Once randomized, the patients will be followed for 6 months with measures of glycemic control and thyroid hormone assessed at entry, 3, and 6 months. At the completion of the study we will compare the glycemic control measurements (fasting glucose, glycosylated hemoglobin) between the levothyroxine treatment group and the observation group using repeated measures ANOVA.

**Progress :** Original PI was reassigned soon after final approval. New PI has not had time to start protocol.

**DETAIL SHEETS FOR PROTOCOLS**

**MADIGAN CANCER INSTITUTE**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/043	<b>Status:</b> Terminated
<b>Title:</b> An Integrated Breast Cancer Information System		
<b>Start Date:</b> 12/17/93	<b>Est. Completion Date:</b> Mar 98	
<b>Department:</b> Madigan Cancer Institute	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> Charlene P. Holt, M.D.		
<b>Associate Investigators:</b> Anne Schur James H. Timmons, MD MAJ Richard R. Gomez, MC MAJ Steven S. Wilson, MC Mark Hinchee	COL Sankaran S. Babu, MC COL Preston L. Carter, MC MAJ Donald V. Smith, MC MAJ Mark E. Robson, MC Sam Stevens, Ph.D. Barbara Fecht	
<b>Key Words:</b> cancer:breast, information systems		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** To develop an integrated breast cancer information and education system.

**Technical Approach:** System components developed under this proposal include: an integrated breast cancer information model and demographic database; an interactive, multi-media kiosk for gathering and maintaining patient demographics and educating the patient about risk factors, diagnosis and treatment approaches; standards-based reporting tools for radiology, pathology, surgery, oncology and radiation therapy that oriented specifically to breast cancer; and a breast cancer data retrieval tool for researchers. The system will be developed over a four year period in a site-independent fashion, enabling it to be acquired and used by other medical centers and hospitals throughout the United States.

**Progress :** Protocol terminated since not funded by DOD Breast Cancer Grant.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF MEDICINE, CARDIOLOGY SERVICE**

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/167		<b>Status:</b> On-going
<b>Title:</b> Heart Failure Management Clinic[colon] A Cost and Benefits Outcomes Analysis Study				
<b>Start Date:</b> 09/15/95			<b>Est. Completion Date:</b> Jul 96	
<b>Department:</b> Medicine, Cardiology Service			<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Maureen A. Arendt, MC				
<b>Associate Investigators:</b> MAJ Phyllis A. Hill, NC			LTC Catherine M. Schempp, MC	
<b>Key Words:</b> heart failure, clinic cost vs benefit				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//

**Study Objective:** The proposed research has been developed to evaluate the effect of an intensive, multidisciplinary outpatient approach to the management of the patient with severe heart failure.

**Technical Approach:** The Heart Failure Management Clinic (HFMC) is designed to improve the outpatient management of patients with symptomatic left ventricular (LV) systolic dysfunction not amenable to surgical correction. These patients have histories of recurrent hospital admissions. Participants will receive ongoing intensive outpatient medical and nursing management combined with structured health education by a multidisciplinary team. Research has shown that with intensive patient education, close outpatient follow-up, and careful manipulation of standard pharmaceutical therapy the number of hospitalizations or emergency room visits can be reduced as well as improvement in the patient's quality of life.

The goal of HFMC is to stabilize the patients' health status. Stability as defined by the number of hospitalizations or emergency room visits will be measured and compared to a comparable group of patients receiving the current standard of care. Functional status and quality of life measurements will be obtained throughout the program.

A total of 60 patients with the diagnosis of congestive heart failure will be enrolled. Patients will be identified by chart review. The first 30 patients that are identified will be placed in the treatment group, the next 30 patients in the control group. The treatment group will attend a series of four one-hour structured education classes on a weekly basis. All subjects will complete questionnaires addressing quality of life issues.

**Progress :** 15 patients have been enrolled in FY95. Three cycles of heart failure education classes have been completed with excellent patient feedback and response. The initial Quality of Life data is still being gathered. Given the small sample size and the natural disease course, it is too early to fully assess the impact on hospitalization.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/169		<b>Status:</b> On-going	
<b>Title:</b> A Multicenter, Randomized, Parallel, Double-Blind Study to Investigate the Safety and Clinical Efficacy of MK-383 Alone and MK-383 in Combination with Heparin vs. Heparin Alone in Patients with ....					
<b>Start Date:</b> 07/21/95			<b>Est. Completion Date:</b> Dec 95		
<b>Department:</b> Medicine, Cardiology Service			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Patrick A. Cambier, MC					
<b>Associate Investigators:</b>					
MAJ Alice M. Mascette, MC		COL Roger F. Chamusco, MC			
MAJ Herman E. Collier III, MC		MAJ Karl C. Stajduhar, MC			
CPT J. Olson, MC		MAJ Maureen A. Arendt, MC			
CPT Michael D. Eisenhauer		CPT Thomas M. Roe, MC			
		CPT John A. McHenry, MC			
<b>Key Words:</b> myocardial infarction, MK-383, Heparin					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		//	

**Study Objective:** 1) To examine the efficacy of MK-383 alone and MK-383 in combination with heparin compared with heparin alone in reducing the combined occurrence of the following clinical events: refractory ischemic conditions (refractory ischemia; hemodynamic instability; or severe, prolonged or repetitive anginal pain at rest requiring urgent invasive intervention within 12 hours of symptom onset), new myocardial infarction or death (through 7 days after initiation of study drugs) in high-risk patients with unstable angina/non-Q-wave myocardial infarction (UAP/NQWMI). the incidence of these endpoints will be examined at 48 hours, through 7 days after initiation of study drug, and at 30 days.

- 2) To examine the safety and tolerability of MK-383 alone and MK-383 in combination with heparin compared with heparin alone in high-risk patients with UAP/NQWMI receiving aspirin and antianginal medications, in the absence of cardiac catheterization.
- 3) to examine the safety and tolerability of MK-383 in combination with heparin compared with heparin alone in an invasive setting(cardiac catheterization).
- 4) To examine the effect of MK-383 in combination with heparin in reducing the maximal extent of angiographically-apparent thrombus compared to heparin alone.

**Technical Approach:** this multicenter, randomized, double-blind study will examine the safety and clinical efficacy of Mk-383 alone and MK-383 in combination with heparin versus heparin alone, in patients with high-risk unstable angina/non-Q-wave myocardial infarction.

Patients meeting entry criteria will be randomized to receive either MK-383 alone (group A), heparin alone (group B), or MK-383 and heparin (group C). Patients will be stratified depending on whether or not they are on a continuous intravenous infusion of heparin at the time of randomization. All patients will receive conventional antianginal therapy consisting for nitrates, betablockers or calcium channel blockers, as deemed necessary by the responsible physician.

During the initial 48-hour period of study drug infusion, patients will not undergo cardiac catheterization unless clinically indicated by development of refractory ischemia or new myocardial infarction. After 48 hours, all patients are expected to



undergo coronary angiography (unless contraindicated) because of their high-risk clinical condition. Study drug may continue, be discontinued and resumed, or discontinued entirely depending upon the findings at time of catheterization. Study drugs may be infused for up to 96 hours (in patients who undergo PTCA/atherectomy no later than Hour 96 while on study drug, the study drug may be administered for up to a total of 108 hours after initiation). All patients will remain under close supervision until 24 hours after discontinuation of the study drug (or until clinically stable). All randomized patients will be followed for 30 days after study drug initiation and also at 6 months. Data to include vital signs, periodic laboratory evaluation, ECG and physical examination findings, adverse clinical events, refractory ischemia, new myocardial infarction, and death will be recorded on all patients. A composite goal of 1260 patients has been established. During the study period, Madigan seeks to enroll between 10 and 25 patients.

Progress : Study just started, no patients yet entered.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/036	<b>Status:</b> Completed
<b>Title:</b> The Influence of Variable Inflation (Oscillation) Techniques on Angioplasty Balloon Deformation and Dilating Force		
<b>Start Date:</b> 11/18/94	<b>Est. Completion Date:</b> Dec 94	
<b>Department:</b> Medicine, Cardiology Service	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Patrick A. Cambier, MC		
<b>Associate Investigators:</b> D. Stewart		
<b>Key Words:</b> variable inflation, angioplasty		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objectives:** This investigation hopes to establish fundamental data regarding actual balloon-generated dilating force, using three distinct balloon materials of varying compliance, when inflated at oscillating pressures both below and above the stated manufacturer's stipulated nominal pressure ranges. In addition, a second investigation will be carried out as to the precise inflated balloon diameter when exposed to the same varying pressures generated in part one.

**Technical Approach:** This protocol will serve to investigate the influence of rapidly varying (oscillating) coronary angioplasty balloon inflation pressures on generated force at a simulated vessel-balloon (dilating) interface. Investigation will center on whether the pressure created by a standard inflation device (indeflator) translates predictably at the dilating interface; with emphasis on three commonly used balloon materials of varying compliance. Further study will be carried out to establish whether such oscillation of inflation pressure alters balloon size in an unexpected fashion than that stated by the manufacturer for a more traditional, sustained inflation pressure technique. Relevant baseline and experimental data were compared among the two study endpoints (dilating force and balloon diameter) in regards to the respective inflation techniques. Baseline and discrete variables will be compared using chi-square analysis, while the Student's T-test will be used to compare continuous variables. A p value  $\leq 0.05$  will determine statistical significance.

**Progress :** A significantly accelerated balloon deformation was shown when using oscillating balloon pressure to inflate the coronary angioplasty balloon. Abstract submitted to Army ACP meeting.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/144		<b>Status:</b> On-going	
<b>Title:</b> BOAT (Balloon versus Optimal Atherectomy)[colon] A Randomized Multicenter Trial of Optimal Directional Coronary Atherectomy versus Balloon Angioplasty					
<b>Start Date:</b> 06/16/95			<b>Est. Completion Date:</b> Jul 96		
<b>Department:</b> Medicine, Cardiology Service			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Patrick A. Cambier, MC					
<b>Associate Investigators:</b> COL Roger F. Chamusco, MC			D. Stewart		
<b>Key Words:</b> BOAT, Atherectomy, balloon vs optimal					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> //

**Study Objectives:** The primary objective of this study is to demonstrate that it is possible to provide larger acute results safely with directional coronary atherectomy (acute residual stenosis  $\leq 15\%$  by QCA) compared to conventional balloon angioplasty, and that such improved results translate into reduced angiographic re-stenosis and diminished clinical need for revascularization.

**Technical Approach:** This is a multi-center, prospective, randomized trial which will enroll 1000 patients with *de novo* lesions in native coronary arteries, who meet entry criteria. Patients will consent to either balloon angioplasty for directional atherectomy who have an indication for coronary revascularization. Upon completion of the procedure, surveillance will be maintained along with a follow-up coronary angiogram 6 months post-procedure. Patients who warrant percutaneous revascularization of multiple lesions in one or more major epicardial coronary arteries (i.e., multi-vessel with multiple lesions) are ineligible. Comparative safety monitoring such as myocardial infarct, need for emergent coronary bypass surgery, and death will also be made. Secondary endpoints including economic impact, and a quality of life comparisons will also be explored. The study endpoints will be drawn from acute and late angiographic (6 month) and late clinical (1 year) outcomes. The primary re-stenosis endpoints, and all secondary endpoints will be analyzed on an intent-to-treat basis, i.e. each outcome will be attributed to the randomized arm regardless of the sequence of procedures that occur.

**Progress :** 3 subjects were entered. Patient enrollment is continuing.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/002	<b>Status:</b> On-going
<b>Title:</b> Efegatran Sulfate as an Adjunct to Streptokinase vs Heparin as an Adjunct to Tissue Plasminogen Activator in Patients with Acute Myocardial Infarction[colon] A Dose-Finding Study		
<b>Start Date:</b> 10/21/94	<b>Est. Completion Date:</b> Jul 95	
<b>Department:</b> Medicine, Cardiology Service	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Patrick A. Cambier, MC		
<b>Associate Investigators:</b>		
COL Roger F. Chamusco, MC	W.D. Weaver	
MAJ Karl C. Stajduhar, MC	MAJ Alice M. Mascette, MC	
MAJ Maureen A. Arendt, MC	MAJ Herman E. Collier III, MC	
LTC John M. Bauman, MC	Steven A. Pace, MD	
CPT Michael A. Rave, MC	K Sapuntzoff	
	MAJ Mark E. Peele, MC	
<b>Key Words:</b> Myocardial Infarction, efegatran, heparin, Streptokinase		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** This study will demonstrate whether the direct acting thrombin inhibitor efegatran, when combined with intravenous streptokinase, can be demonstrated to produce equal or superior 90-minute coronary patency and lower reocclusion rates than heparin and recombinant tissue plasminogen activator (t-PA) alone in acute myocardial infarction.

**Technical Approach:** Patients will be randomized to receive either TPA and heparin or streptokinase and efegatran in an attempt to quickly dissolve the clot. TPA will be given IV over 90 minutes for a total dose not to exceed 100mg. The heparin will be given IV as a 5000 unit bolus followed by 1000 units/hour for 72 to 96 hours. Streptokinase (1.5 million units) will be given IV over 60 minutes. Efegatran will be given IV (0.3 mg/kg/hr) for 72 to 96 hours. To verify the vessel is opening, a heart catheterization will be performed.

**Progress :** 13 subjects were entered. Enrollment is ongoing.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 93/103	<b>Status:</b> Terminated		
<b>Title:</b> A Randomized, Double-Blind, Placebo-Controlled Study of the Efficacy and Safety of RheothRx Injection (Polaxamer 188) in Patients with Suspected Acute Myocardial Infarction				
<b>Start Date:</b> 05/07/93	<b>Est. Completion Date:</b> May 94			
<b>Department:</b> Medicine, Cardiology Service	<b>Facility:</b> MAMC			
<b>Principal Investigator:</b> COL Roger F. Chamusco, MC				
<table style="width: 100%; border: none;"> <tr> <td style="width: 50%; vertical-align: top;"> <b>Associate Investigators:</b>            COL Joseph A. Paris, MC            MAJ Doreen Saltiel, MC            MAJ James C. Mullin, MC            MAJ Mark E. Peele, MC            CPT Scott A. Sample, MC         </td> <td style="width: 50%; vertical-align: top;">           LTC John M. Bauman, MC            MAJ Alice M. Mascette, MC            MAJ Karl C. Stajduhar, MC            MAJ Patrick A. Cambier, MC            CPT Michael A. Rave, MC         </td> </tr> </table>			<b>Associate Investigators:</b> COL Joseph A. Paris, MC MAJ Doreen Saltiel, MC MAJ James C. Mullin, MC MAJ Mark E. Peele, MC CPT Scott A. Sample, MC	LTC John M. Bauman, MC MAJ Alice M. Mascette, MC MAJ Karl C. Stajduhar, MC MAJ Patrick A. Cambier, MC CPT Michael A. Rave, MC
<b>Associate Investigators:</b> COL Joseph A. Paris, MC MAJ Doreen Saltiel, MC MAJ James C. Mullin, MC MAJ Mark E. Peele, MC CPT Scott A. Sample, MC	LTC John M. Bauman, MC MAJ Alice M. Mascette, MC MAJ Karl C. Stajduhar, MC MAJ Patrick A. Cambier, MC CPT Michael A. Rave, MC			
<b>Key Words:</b> myocardial infarction, RheothRx				
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 09/02/94		

**Study Objective:** (1) To evaluate the effect of RheothRx Injection, if any, on resultant myocardial infarct size, compared to placebo, when given to patients with suspected AMI who are not treated acutely with thrombolytic therapy or direct percutaneous transluminal coronary angioplasty (PTCA). (2) To assess the safety of RheothRx Injection in this patient population.

**Technical Approach:** This is a multicenter, randomized, double-blind, placebo-controlled evaluation of the safety and efficacy of RheothRx Injection in patients with suspected acute myocardial infarction who are not eligible to receive thrombolytic therapy or acute, direct PTCA. Such patients presenting with ongoing symptoms suspicious of AMI of at least 30 minutes in duration but within 6 hours since onset will be considered for enrollment in the study. Two hundred and fifty (250) patients will be enrolled at approximately ten to fifteen centers. Eligible patients will receive a 48 hour intravenous infusion of either RheothRx injection or placebo. All patients will receive aspirin throughout the hospitalization. Randomization to RheothRx injection or placebo will be stratified by the initial type of EKG abnormality (ST elevation or ST depression/ T wave inversion/ bundle branch block/ non-specific intraventricular conduction delay present at the time of enrollment and by the enrolling center. The safety of RheothRx will be evaluated using periodic laboratory tests, assessments of vital signs, physical examination, collection of adverse experiences, bleeding complications, and disease-related events. Efficacy will be assessed by measures of myocardial infarct size, left ventricular ejection fraction, and clinical outcome. Infarct size will be measured on days 5 - 10 by single photon emission computer tomography using technetium 99m sestamibi. Ejection fraction will be measured on days 5 - 10 by radionuclide ventriculography. Clinical outcome will be assessed by monitoring the occurrence of prospectively specified clinical events during the six-month period following randomization. Two composite scores of efficacy will be computed from the recorded events.

**Progress :** 1 subjected was entered this FY, 24 subjects in total have been entered at MAMC. 1 death at MAMC, September 1994. Study has been closed do to numerous serious adverse events (deaths).

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/018		<b>Status:</b> Completed	
<b>Title:</b> Cardiac Dimensions in Female Athletes					
<b>Start Date:</b> 11/06/92			<b>Est. Completion Date:</b> Jun 93		
<b>Department:</b> Medicine, Cardiology Service			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Alice M. Mascette, MC					
<b>Associate Investigators:</b> MAJ Karl C. Stajduhar, MC			MAJ Patrick A. Cambier, MC		
<b>Key Words:</b> cardiac dimensions, female athletes					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		//	

Study Objective: To non-invasively obtain cardiac dimensions in women engaged in regular vigorous aerobic and power training.

Technical Approach: Twenty volunteer female athletes engaged in regular vigorous aerobic activity and twenty volunteer female athletes engaged in regular power sports will undergo standard two dimensional echocardiography. Standard measurements of left ventricular wall thickness (septum and posterior wall) and cavity dimensions will be measured on-a-line from the parasternal long axis view at the time of study. The technical staff will be blinded as to the exercise interview conducted at the time of recruitment. The echocardiograms will be overread by two staff cardiologists and measurements recorded. Differences will be resolved by averaging results. A cohort of age, height, and weight-matched controls will be recruited and mean dimensions from their studies statistically compared with the athletes using the ANOVA test.

Progress : Fifty subjects were enrolled in this study at MAMC. Data analysis showed a statistically significant increase in left ventricular dimensions in aerobic and anaerobic athletes as compared to controls. There was an upward trend in wall thickness anaerobic athletes, but was not statistically significant for the aerobic athletes.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/099		<b>Status:</b> On-going	
<b>Title:</b> The Effect of Coronary Angiography on Subsequent Left Ventriculography					
<b>Start Date:</b> 05/06/94			<b>Est. Completion Date:</b> Sep 94		
<b>Department:</b> Medicine, Cardiology Service			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Alice M. Mascette, MC					
<b>Associate Investigators:</b>			COL Roger F. Chamusco, MC		
<b>Key Words:</b> coronary, angiography, ventricle:left					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
<b>Periodic Review:</b>					//

**Study Objective:** To evaluate the results of left ventriculography performed after coronary arteriography, compared to that performed before, in patients undergoing cardiac catheterization at Madigan.

**Technical Approach:** Patients scheduled to undergo elective cardiac catheterization will have an additional left ventriculogram performed at the time of heart catheterization. Left ventriculography performed before coronary arteriography will be compared with left ventriculography performed after coronary arteriography using the patient as his/her own control. Left ventriculograms will be analyzed by blinded observers for overall ejection fraction and regional wall motion analysis using existing computerized programs and compared using paired t test

**Progress :** Four subjects have been enrolled in this study at MAMC. Data for wall motion was difficult to collect with present computer equipment. The study has been temporarily suspended pending installment of a new cath lab computer system.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/180		<b>Status:</b> On-going	
<b>Title:</b> Stress Echocardiography in the Evaluation of Asymptomatic Aircrew Members for Significant Coronary Artery Disease					
<b>Start Date:</b> 08/18/95			<b>Est. Completion Date:</b> Jun 96		
<b>Department:</b> Medicine, Cardiology Service			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ James P. Olson, MC					
<b>Associate Investigators:</b> MAJ Maureen A. Arendt, MC			E.M. Collier		
<b>Key Words:</b> Coronary artery disease, stress echocardiography					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
<b>Periodic Review:</b>					//

**Study Objectives:** To compare the sensitivity and specificity of exercise echocardiography and exercise <sup>201</sup>Tl scintigraphy in the evaluation of asymptomatic aircrew members who have been referred to the Cardiology Service for suspected coronary artery disease.

**Technical Approach:** Our study population will consist of 20-40 active duty US Army aviators. Subjects will be those aviators who have been referred to the Cardiology Service for cardiac catheterization to determine the presence or absence of significant coronary artery disease. Each subject will undergo an exercise echocardiogram and exercise <sup>201</sup>Tl scintigraphy prior to diagnostic angiography. We will also determine the presence or absence of fluoroscopic or cineangiographic calcification in the coronary artery distribution. Images will be interpreted by two experience cardiologists who are blinded to thallium, echocardiographic and clinical data. For this study, significant coronary artery disease will be defined as one or more stenosis of equal to or greater than 50% in any major coronary artery, including large diagonal and marginal branches. The study will also be defined as abnormal if no lesion is equal to or greater than 50% but the aggregate of lesions identified is equal to or greater than 120%. Data will be collected from each case. Numerical variables will be compared using t-test and yes/no or normal/abnormal variables will be compared using the chi-square test. We will then determine the sensitivity, specificity and predictive value to each diagnostic modality.

**Progress :** Patient accrual has not begun since protocol was just approved.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/126	<b>Status:</b> Completed
<b>Title:</b> Potassium Channel Gene Expression in States of Thyroid Dysfunction and Amiodarone Treatment		
<b>Start Date:</b> 06/10/94	<b>Est. Completion Date:</b>	
<b>Department:</b> Medicine, Cardiology Service	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Mark E. Peele, MC		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> Thyroid, potassium, amiodarone, Animal Study		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** To study the expression of the potassium channels RK3(Kv1.5) in rat heart. The effects of amiodarone, thyroid hormone deficiency, and thyroid hormone excess upon steady state messenger RNA levels as determined by northern analysis.

**Technical Approach:** Sixteen adult male rats will be divided into four equal experimental groups. T3 group will receive daily intraperitoneal (IP) injections of T3 200 mcg/kg for 2 weeks prior to sacrifice. Hypothyroid group will receive a 0.1% merthimazole solution ad lib in their drinking water supply for 4 weeks prior to sacrifice. Amiodarone group will receive daily IP injections of amiodarone 20 mg/kg for 4 weeks prior to sacrifice. Control animals will receive standard rat chow. Animals will be euthanized by standard lab practice with collection of sera for determination of thyroid stimulating hormone levels and harvesting of myocardium. Total cellular RNA will be collected by standard methodology. Size fractionated by electrophoresis on 1% agarose denaturing formaldehyde gels. RNA will be capillary transferred to charged nylon membranes and UV light fixed after formaldehyde neutralization.; Samples of rat heart total cellular RNA will serve as template for first strand synthesis of cDNA. Restriction fragment analysis of amplified RK3 (Kv1.4) and RK4 (Kv1.5) DNA will be performed on 1% agarose gels to confirm cDNA identity. Statistical significance of study variables between experimental groups will be determined by ANOVA.

**Progress :** 18 rats were used in data analysis, no rats were entered this FY. Amiodarone treatment was found to increase rat ventricular action potential duration and transcriptional down regulation of the Kv1.5 gene.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/115		<b>Status:</b> Completed	
<b>Title:</b> Evaluation of Morphologic Variables Related to Adverse Outcome During Coronary Angioplasty of the Right Coronary Artery					
<b>Start Date:</b> 04/21/95			<b>Est. Completion Date:</b> Jul 95		
<b>Department:</b> Medicine, Cardiology Service			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Michael A. Rave, MC					
<b>Associate Investigators:</b> D. Stewart Cindy B. Lee, MD			MAJ Patrick A. Cambier, MC J. Chambers W.G. Grown		
<b>Key Words:</b> Angioplasty, right coronary artery, morphologic variables					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//	

**Study Objective:** To determine the morphologic, procedural, and clinical characteristics specific to the right coronary artery which are predictive of adverse outcome during balloon angioplasty of atherosclerotic lesions in this vessel.

**Technical Approach:** This study is as retrospective review of coronary angioplasty cases done at the University of Washington, Seattle, and Madigan Army Medical Center from September 1991 until March 1995. All cases of coronary angioplasty of the right coronary artery will be identified and patient data sheets and angiography and procedural cines will be obtained. Clinical and morphological variables will be assessed and recorded on the protocol worksheet using consensus definitions. All cines will be reviewed by at least two experienced angiographers. At the conclusion of the data collection, clinical variables will be assessed for an association with the following endpoints: a) urgent CABG; b) urgent CABG + coronary stent placement; c) urgent CABG + coronary stent placement + major dissection; and d) all the above plus use of more than one coronary catheter required for acceptable result. Variables will be assessed for independent association using Chi-square analysis for presentation as relative risk with 95% confidence intervals. It is then anticipated that a stepwise multiple regression model will be created to produce a risk score which would then be evaluated internally or possibly used for future prospective studies. For most variables a population size of 500 lesions will give sufficient power to give meaningful results.

**Progress :** 489 cases were reviewed. Univariate predictors of Level I endpoints (abrupt closure) included lesion length >10 millimeters, eccentricity, and non-smooth morphology. In multivariate analysis, eccentricity and length were independently predictive. Univariate predictors of Level II endpoints (Level I or the requirement for perfusion balloon) include proximal vessel location, eccentricity, proximity of major branch, length >10 millimeters, quantitative severity, and single lesion present in the artery. Multivariate predictors were length, eccentricity, and presence of single lesion. Univariate predictors of Level III endpoints (Level II or any use of more than one angioplasty balloon) were numerous; length, lesion angle >60 degrees, diffuse vessel involvement, and isolated lesion were independently significant.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/027		<b>Status:</b> Completed	
<b>Title:</b> Comparison of Intravenous Adenosine With Exercise in Thallium-201 SPECT in Patients With Left Bundle Branch Block					
<b>Start Date:</b> 12/04/92			<b>Est. Completion Date:</b> Jun 94		
<b>Department:</b> Medicine, Cardiology Service			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Michael A. Rave, MC					
<b>Associate Investigators:</b> COL Roger F. Chamusco, MC LTC John M. Bauman, MC			MAJ Doreen Saltiel, MC MAJ Stephen E. Budd, MC		
<b>Key Words:</b> left bundle branch block, adenosine, exercise					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$3000.00
					<b>Periodic Review:</b> //

**Study Objective:** To determine if the diagnostic value of adenosine in conjunction with thallium-201 SPECT imaging is improved over standard thallium exercise testing in patients with left bundle branch block.

**Technical Approach:** Patients referred for ischemic heart disease will receive pharmacologic stress with adenosine at 0.14 mg/kg and an exercise thallium-201 SPECT imaging (using a symptom limited Bruce exercise protocol) approximately one week apart. A cardiac catheterization will be performed within four weeks of the scans. All thallium SPECT images will be evaluated by two experienced observers blinded to the clinical history and angiography results. The radio nuclide studies will not be matched for the same patient until all studies have been read. The cineangiograms will be reviewed by a single reviewer blinded to the results of the thallium imaging. At the end of enrollment the results of the imaging studies and cardiac cath lab evaluations will be paired up and analyzed.

**Progress :** Completed data on ten patients demonstrate one patient with obstructive coronary lesions who had corresponding abnormalities on both imaging studies. The remaining nine patients had no obstructive coronary lesions. All of these had normal adenosine thallium studies while seven of nine had abnormal exercise thallium scans. Specificity of adenosine for detection of coronary artery disease was 100% compared with 2.2% in exercise thallium ( $p=0.1$ ). These results are consistent with previously published data and argue against use of exercise in conjunction with radionuclide imaging in patients with left bundle branch block.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/043		<b>Status:</b> On-going	
<b>Title:</b> Effects of Chronic Smoking and Transdermal Nicotine Replacement Therapy on Hemostatic Function in Humans					
<b>Start Date:</b> 03/17/95			<b>Est. Completion Date:</b> Jun 95		
<b>Department:</b> Medicine, Cardiology Service			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Thomas M. Roe, MC					
<b>Associate Investigators:</b>			CPT Scott A. Sample, MC		
<b>Key Words:</b> smoking, nicotine replacement therapy, hemostasis					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		//

Study Objectives: To determine the effects of smoking and transdermal nicotine therapy on the hemostatic function of healthy men and women.

Technical Approach: Healthy male and female volunteers undergoing routine periodic physical examination or participating in smoking cessation programs using nicotine replacement therapy will donate blood samples. The blood will be prepared for assay measurement of tissue plasminogen activators, tissue plasminogen activator inhibitor 1, fibrinopeptide A, platelet factor IV, beta thromboglobulin and thrombin-antithrombin III complex. 120 subjects will be included and will be divided into control, smoking and nicotine replacement therapy groups. Assays will be performed in duplicate for each specimen tested. The data will then undergo standard statistical analysis to determine statistical significance.

Progress : 68 subjects have been enrolled. Smoking activates the coagulation system more than nicotine alone; gender differences in hemostasis are diminished by smoking, and smokeless tobacco causes platelet activation and not fibrin activation.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/042	<b>Status:</b> Terminated
<b>Title:</b> Distribution of Delayed Rectifier Potassium Channel (Kv1.5) Gene Expression in Rat Cardiac Tissue Localized by In Situ Detection of PCR-amplified DNA		
<b>Start Date:</b> 01/23/95	<b>Est. Completion Date:</b> May 95	
<b>Department:</b> Medicine, Cardiology Service	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Scott A. Sample, MC		
<b>Associate Investigators:</b>		MAJ Mark E. Peele, MC
<b>Key Words:</b> DNA, gene expression, potassium, cardiac tissue, Animal Study, rat		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objectives:** The objective of this study is to determine if the expression of delayed rectifier potassium channel gene (Kv1.5) will demonstrate regional variations in cardiac action potential within the rat heart.

**Technical Approach:** The delayed rectifier potassium channel gene (Kv1.5) in rats controls the movement of potassium in and out of the cells of the body. We plan to study the expression and control of this gene in the rat heart by using molecular biology. This descriptive study will use Polymerase Chain Reaction technology to examine the rate and location of Kv1.5 expression by reverse transcription and PCR amplification of an RNA preparation from formalin-fixed, paraffin-embedded rat heart tissue. A total of 8 young, male rats will be used. The rats will be euthanitized using Isoflurane after 1-2 weeks and the heart tissue will be collected at necropsy and placed in 10% buffered formalin.

**Progress :** 6 subjects have been entered. Attempted in situ PCR without success to identify potassium channel gene expression.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/068	<b>Status:</b> On-going
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**Title:** A Double-Blind, Placebo Controlled, Randomized, Dose Response Study of Oral dl-Sotalol Hydrochloride for the Maintenance of Sinus Rhythm in Subjects with Prior Symptomatic Atrial Fibrillation or ....

**Start Date:** 02/17/95

**Est. Completion Date:** Apr 97

**Department:** Medicine, Cardiology Service

**Facility:** MAMC

**Principal Investigator:** MAJ Karl C. Stajduhar, MC

**Associate Investigators:**

COL Roger F. Chamusco, MC

MAJ Herman E. Collier III, MC

CPT Michael A. Rave, MC

CPT Scott A. Sample, MC

CPT Thomas M. Roe, MC

MAJ Patrick A. Cambier, MC

MAJ Alice M. Mascette, MC

MAJ Maureen A. Arendt, MC

MAJ Mark E. Peele, MC

MAJ James P. Olson, MC

CPT Michael D. Eisenhauer

**Key Words:** Sinus rhythm, atrial fibrillation, dl-Sotalol Hydrochloride

**Accumulative**

**MEDCASE Cost:** \$0.00

**Est. Accumulative**

**OMA Cost:** \$0.00

**Periodic Review:**

//

**Study Objective:** To evaluate the efficacy and safety of oral dl-sotalol Hcl in subjects with prior symptomatic atrial fibrillation (AFIB) or atrial flutter (AFL) for the maintenance of sinus rhythm.

**Technical Approach:** Multicenter, double-blind, placebo controlled, randomized, dose response study to evaluate the efficacy and safety of oral dl-sotalol Hcl in subjects with prior symptomatic atrial fibrillation (AFIB) or atrial flutter (AFL) for the maintenance of sinus rhythm. Six subjects will be randomly assigned to receive one of the three fixed dose regimens of dl-sotalol Hcl (80 mg, 120 mg or 160 mg) or placebo administered every 12 hours orally. The study will consist of double-blind and open-label phases. Treatment will last for 12 months. In the analysis of time to AFIB/AFL, the log-rank test will be used. The proportions of subjects free of AFIB/AFL for two treatments groups will be compared at 6 months and 12 months using the product-limit estimates. The corresponding variances will be computed using Greenwood's formula. This method adjusts for dropouts or censored data.

**Progress :** 7 subjects have been entered, subject accrual continues.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/040		<b>Status:</b> Terminated	
<b>Title:</b> The Effect of Oral D-Sotalol on Mortality in Patients With Atherosclerotic Coronary Heart Disease and Left Ventricular Dysfunction					
<b>Start Date:</b> 12/17/93			<b>Est. Completion Date:</b> Jul 95		
<b>Department:</b> Medicine, Cardiology Service			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Karl C. Stajduhar, MC					
<b>Associate Investigators:</b>					
COL Roger F. Chamusco, MC			MAJ James P. Olson, MC		
MAJ Doreen Saltiel, MC			MAJ Alice M. Mascette, MC		
MAJ James C. Mullin, MC			COL Joseph A. Paris, MC		
MAJ Mark E. Peele, MC			MAJ Patrick A. Cambier, MC		
CPT Scott A. Sample, MC			CPT Michael A. Rave, MC		
<b>Key Words:</b> coronary disease, oral d-Sotalol, mortality					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		//	

**Study Objective:** To determine whether d-sotalol, a Class III antiarrhythmic agent, will reduce total (all-cause) mortality compared to placebo in patients with left ventricular dysfunction (resting LV ejection fraction  $\leq 40\%$  and CHD).

**Technical Approach:** This is a multicenter, randomized, double-blind, placebo-controlled trial in patients with LV dysfunction and atherosclerotic coronary heart disease (CHD). This study will consist of a screening and double blind phase. The screening phase will determine if the volunteers meet the enrollment criteria. Those qualifying for the double-blind phase will receive either d-sotalol or placebo for eighteen months and be monitored clinically as well as by standard laboratory methods. Data will be analyzed by the sponsor.

**Progress :** Protocol has been terminated by sponsor with no patients being entered at MAMC.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF MEDICINE, CRITICAL CARE  
SERVICE**



### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/055		<b>Status:</b> Completed
<b>Title:</b> American Academy of Neurology Critical Care Skills Workshop (pig, yorkshire)				
<b>Start Date:</b> 01/23/95		<b>Est. Completion Date:</b> May 95		
<b>Department:</b> Medicine, Critical Care Svc		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Lewis L. Low, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> training:neurology, pig,Animal Study				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//

**Study Objective:** To allow physicians to 1) identify arterial, pulmonary, pulmonary capillary wedge, and intracranial waveforms by measuring them in animals. 2) The students will further develop these skills by learning to calculate cardiac output and pulmonary & systemic resistances by measuring the hemodynamic parameters from the monitors. 3) The students will be introduced to advanced techniques for airway management via fiberoptic bronchoscopy guided endotracheal intubation.

**Technical Approach:** Unlike in the past, neurologists are now commonly asked to care for ICU patients and must have a working knowledge of current monitoring techniques and their use in the ICU. The students that are taking this course are being trained to perform techniques that have only been developed over the past ten years, after many of them completed their initial medical training. This is a dynamic exercise to study, and by experimentation, demonstrate some of the more important factors responsible for control of blood pressure and cardiac function. Specifically, students will gain experience with a simple surgical model, evaluate normal physiology, observe the effects of inotropic, vasopressor, and vasodilator drugs. Additionally, they will learn about various techniques to monitor intracranial pressure and effectively control a patient's airway. All invasive procedures will be conducted by either course faculty or LASS staff. No students will perform invasive procedures.

**Progress :** Workshop was completed successfully.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/029	<b>Status:</b> On-going
<b>Title:</b> A Prospective Study Using the Airway Occlusion Pressure (PO.1) To Predict the Outcome of Weaning From Mechanical Ventilation		
<b>Start Date:</b> 12/17/93	<b>Est. Completion Date:</b> May 94	
<b>Department:</b> Medicine, Critical Care Svc	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Lewis L. Low, MC		
<b>Associate Investigators:</b> MAJ George N. Giacoppe Jr., MC CPT Jeremy R. Blanchard, MC		
MAJ James D. Pike, MC MAJ Francis J. Landry, MC		
<b>Key Words:</b> ventilation, airway occlusion pressure		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

Study Objective: The main objective of this study is to ascertain the usefulness of the PO.1 as a weaning parameter in predicting success or failure of patients upon extubation. The secondary objective is to validate the Rapid Shallow Breathing Index as described by Yang and Tobin.

Technical Approach: Weaning parameters will be obtained and documented by a Respiratory Care Practitioner (RCP) on patients in the surgical and medical ICU at MAMC. Individual progress toward weaning and extubation will be determined by the primary physician/team. When it is determined the patient is ready for extubation, a second set of weaning parameters will be obtained immediately prior to extubation. Weaning parameters will only be collected on patients at rest and who have not been stimulated within the prior 10 minutes. The parameters will be obtained by utilizing the Respiratory Mechanics Package on the Infrasonics Adult Star as required by MAMC policy. Only the data obtained from patients on the Infrasonic Adult STAR mechanical ventilator will be used so that our results are reproducible since other available ventilators do not easily measure the PO.1. The first 50 patient's will be used to form ROC curves to develop threshold values for the prediction of success or failure of extubation which can then be prospectively applied. A successful weaning/extubation will be defined as one in which the patient does not have to be reintubated within 24 hours.

Progress : 70 subjects have been entered. Data analysis is pending.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/005	<b>Status:</b> On-going
<b>Title:</b> Effect of Empiric Low-Dose Amphotericin B or Fluconazole on the Development of disseminated Candidiasis in an Intensive Care Unit		
<b>Start Date:</b> 10/01/93	<b>Est. Completion Date:</b> Jul 95	
<b>Department:</b> Medicine, Critical Care Svc <b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Joseph S. Pina, MC		
<b>Associate Investigators:</b> MAJ Lewis L. Low, MC CPT Gregory S. Witkop, MC		
<b>Key Words:</b> candidiasis, amphotericin B, Fluconazole		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** To determine the efficacy of low-dose amphotericin B (AmB) or Fluconazole (Flu) in preventing the development of disseminated candidiasis.

**Technical Approach:** There will be two study groups, one receiving low-dose AmB 0.3 mg/kg/day, and the other receiving Flu 200 mg IV q24h. Those patients who do not receive either regimen will serve as the control group and will receive the standard of care given in the "community", i.e. treat local Candida infections with local treatment until dissemination occurs, whereby full dose AmB is employed. Hematologic, chemistry, and microbiologic monitoring will be performed. The two treatment groups will be compared to the control group, utilizing the Chi-square test. There will be no comparison between the two treatment groups themselves. Survival analysis will be used to compare the time until appearance of disseminated candidiasis between treatment groups.

**Progress :** 21 total subjects entered, 12 in FY 95. Study is continuing to enroll subjects.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/159		<b>Status:</b> Terminated
<b>Title:</b> Randomized Trial of E5 Antiendoxin Monoclonal Antibody in Patients With Severe Sepsis				
<b>Start Date:</b> 08/06/93			<b>Est. Completion Date:</b> Nov 94	
<b>Department:</b> Medicine, Critical Care Svc			<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Anthony S. Sado, MC				
<b>Associate Investigators:</b>			MAJ Kathleen M. Sheehan, MC	
<b>Key Words:</b> sepsis, monoclonal antibody				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//

**Study Objective:** To determine whether the administration of E5 enhances survival in patients with severe sepsis due to documented gram-negative infection when compared to placebo.

**Technical Approach:** Hospitalized patients > 18 years who have a documented serious gram negative infection within 2 calendar days prior to entry will be screened for clinical signs of sepsis. Patients will be randomized to receive standard antibiotic therapy and E5 (monoclonal antibody) versus standard antibiotic therapy. E5 will be given over 1 hour on days one and two and the patients will be monitored for any adverse effects. All patients will be followed for survival at days 14 and 28.

**Progress :** No patients were entered at MAMC due to restraint of having to give their own consent.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF MEDICINE, ENDOCRINOLOGY**  
**SERVICE**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/046		<b>Status:</b> Completed	
<b>Title:</b> A Randomized, Double-Blind, Placebo-Controlled, Parallel Titration Which Explores the Safety and Efficacy of Glipizide GITS Tablets in A Broad Range of Patients With NIDD					
<b>Start Date:</b> 12/17/93			<b>Est. Completion Date:</b> Jul 95		
<b>Department:</b> Medicine, Endocrinology Svc			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL David L. Bunner, MC					
<b>Associate Investigators:</b> LTC Daniel H. Knodel, MC CPT Barrett L. Chapin, MC			COL Robert E. Jones, MC MAJ Robert M. Tuttle, MC CPT Lloyd D. Hancock, MC		
<b>Key Words:</b> diabetes, NICC, glipizide					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		//	

Study Objective: 1) To evaluate the safety and efficacy of the Glipizide GITS tablet, a once-a-day formulation of Glipizide, in a broad spectrum of Non-Insulin Dependent Diabetes Mellitus patients. In addition, an evaluation of hypoglycemia and hyperglycemia will be made via questionnaires in association with documented home glucose measurements.

Technical Approach: Fifteen patients from MAMC will be evaluated for a maximum of 16 weeks. The study will consist of a 1-week washout from current oral sulfonylureas (if applicable); a 3 week, single-blind placebo phase; a 4-week, double-blind titration phase; and an 8-week, double-blind efficacy phase. Patients who have been on diet alone for at least 3 months and are considered to be dietary failures may enter the placebo phase directly. Following participation in this study, patients may be eligible for entry into a long-term, open-label extension study.

Progress : Nineteen patients were randomized. One patient transferred before completing the study. Eighteen completed the protocol and continue to be followed with the Endocrinology Service.

### Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 94/132

**Status:** Completed

**Title:** Does Pretreatment with Propylthiouracil or Methimazole Decrease the Effectiveness of Radioactive Iodine Therapy in Graves Disease?

**Start Date:** 08/05/94

**Est. Completion Date:** Jul 94

**Department:** Medicine, Endocrinology  
Svc

**Facility:** MAMC

**Principal Investigator:** CPT Lloyd D. Hancock, MC

**Associate Investigators:**  
LTC Homer J. Lemar Jr., MC  
Troy H. Patience, B.S.

MAJ Robert M. Tuttle, MC  
LTC John M. Bauman, MC

**Key Words:** Graves' disease, propylthiouracil, methimazole, radioactive iodine

**Accumulative**

**Est. Accumulative**

**Periodic Review:**

**MEDCASE Cost:** \$0.00

**OMA Cost:** \$0.00

//

**Study Objective:** Our objective is to determine whether pretreatment with antithyroidal medications significantly effects the therapeutic efficacy of radioactive iodine used in the treatment of Graves disease.

**Technical Approach:** We plan to review all cases of RAI administered at MAMC between 1960 and 1994 to identify all cases of Graves disease treated with RAI. Using the clinical records we will determine which patients received antithyroidal agents. In all patients in whom at least one year follow-up data is available, we will compare treatment failure rates in those receiving RAI alone with those receiving RAI after pretreatment with PTU or methimazole. Demographic parameters will be evaluated in an effort to find any selection bias in those patients receiving antithyroidal drug pretreatment. It is hoped that this retrospective study will clarify whether pretreatment with antithyroidal drugs has an effect on the therapeutic efficacy of RAI.

**Progress :** 116 subjects entered. Manuscript submitted for Fellow's Research Award. Treatment with PTU in this group of patients did not significantly diminish the effectiveness of RAI therapy although the rate of RAI failure was nearly twice as high after previous PTU therapy than with RAI therapy alone.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 92/069		<b>Status:</b> Terminated	
<b>Title:</b> Phospholipid Composition of Human Epididymal and Ejaculated Spermatozoa					
<b>Start Date:</b> 06/05/92			<b>Est. Completion Date:</b> Jun 94		
<b>Department:</b> Medicine, Endocrinology Svc			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL Robert E. Jones, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> spermatozoa, phospholipid, epididymus					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		//	

**Study Objective:** (1) To determine the quantitative changes in sperm plasma membrane phospholipids and phospholipid-bound fatty acids as they traverse the epididymis and (2) to compare these results to the values obtained from ejaculated sperm.

**Technical Approach:** Thirty fertile volunteers undergoing elective vasectomy will be asked to provide two semen samples prior to surgery. During the surgical procedure, sperm will be obtained by milking the proximal end of the vas deferens and epididymis. The samples will be washed in a calcium free buffer, and the phospholipids will be extracted using chloroform and methanol. The extracted phospholipids will be kept under a nitrogen atmosphere at -70 degrees centigrade until they are assayed. Pooling of samples may be necessary to ensure adequate detection of minor phospholipids and fatty acids. The position and bonding of fatty acids will be determined through a combination of enzymatic and chemical hydrolysis. Quantification of fatty acids will be performed using gas chromatography, and either high performance liquid chromatography or quantitative thin layer chromatography to identify phospholipids. Results will be expressed by normalizing values to sperm number, to phospholipid phosphorous, or as a percentage of total sperm lipids of a similar class. The data will be handled using descriptive statistics, and the statistical analysis will employ an unpaired t test or an ANOVA when appropriate.

**Progress :** Terminated due to inability to obtain epididymal sperm.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 87/023		<b>Status:</b> On-going	
<b>Title:</b> Investigations into the Mechanisms of Phospholipid Synthesis in Human Spermatozoa					
<b>Start Date:</b> 11/21/86			<b>Est. Completion Date:</b> Dec 87		
<b>Department:</b> Medicine, Endocrinology Svc			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL Robert E. Jones, MC					
<b>Associate Investigators:</b> CPT Kevin J. Carlin, MC			MAJ Charles J. Hannan, MC Stephen R. Plymate, M.D.		
<b>Key Words:</b> spermatozoa,phospholipid synthesis					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$1600.00
					<b>Periodic Review:</b> 10/21/88

**Study Objective:** To determine if sperm can replenish phospholipids after they have been partially hydrolyzed to the lyso-forms by the action of phospholipases A2 or A1 and to attempt to identify and characterize sperm acyl transferase.

**Technical Approach:** Acyl transferase, acyl CoA:1-acyl-sn-glycero-3-phosphocholine O-acyl transferase will be screened by coincubating human sperm with labeled fatty acids, CoASH, ATP, Mg<sup>2+</sup>, and Tris. The reaction will be terminated by delipidating the sperm with CHCl<sub>3</sub>: MeOH, and the organic phase will be chromatographed on silica gel TLC plates. These plates will be developed and spots will be scraped and counted. If the labeled fatty acid is found to be contained within a phospholipid region, cofunctioning of ligase and acyl transferase will be assumed to occur. Studies to characterize acyl transferase activity will be performed using an assay based on the liberation of CoASH which reacts with DTNB, resulting in a change in absorption at 414 nm. Either palmitoyl or docosahexaenoyl CoA will be used as the acyl donor to lyso-phosphatidyl choline. The conversion of lyso-phosphatidyl choline to phosphatidyl choline will be chromatographed. This assay will be optimized for pH, ionic strength, substrate levels and amount of enzyme before kinetic constants are determined. For carnitine-dependent transacylation, D, L-palmitoyl carnitine and lyso-phosphatidyl choline will be coincubated with washed sperm, delipidated and the products chromatographed as above. If the amount of lyso-phosphatidyl choline declines while phosphatidyl choline increases, a carnitine dependent mechanism will be presumed to exist. Alternatively, carnitine dependency could be screened by using 3H-palmitoyl carnitine to look for labeled phosphatidyl choline formation. The effect of 22:6 on 16:0 incorporation into phospholipids will be assessed by incubating unlabeled 22:6 with 3H-16:0 and following the appearance of 16:0 in phosphatidyl choline. Conversely, the effect of 16:0 on 14C-22:6 will be studied.

**Progress :** No further work was done this FY. Manuscript in preparation.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 92/093	<b>Status:</b> On-going
<b>Title:</b> Hyperactivation in Cryopreserved Spermatozoa[colon] Effects of Progesterone and Various Membrane-Active Agents		
<b>Start Date:</b> 08/07/92	<b>Est. Completion Date:</b>	
<b>Department:</b> Medicine, Endocrinology Svc	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> COL Robert E. Jones, MC		
<b>Associate Investigators:</b> CPT M. Ahmed, MC CPT Wilma I. Larsen, MC CPT David H. Harrison, MC	COL Robert E. Jones, MC CPT J. Olson, MC CPT Colleen C. Foos, MC A.Y. Jones	
<b>Key Words:</b> spermatozoa, cyropresavation, hyperactivation		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** To determine the optimal incubation buffer (human follicular fluid versus a synthetic, defined media, both supplemented with varying concentrations of progesterone) to induce hyperactivated motility in cryopreserved human sperm. Once the optimal hyperactivation conditions are determined, the effects of a variety of different classes of agents (calcium channel blockers, free fatty acids, platelet activating factor, and the synthetic phospholipase A2 inhibitors, U73,343 and U73,122,) on hyperactivated motility and motility during capacitation will be assessed.

**Technical Approach:** Cryopreserved sperm will be counted via computer assisted semen analysis (CASA), washed, reassessed, and incubated in a capacitating buffer containing Ham's F10 with 3.5% bovine serum albumin. After capacitation, the sperm will be incubated in similar media supplemented with diluted (1/20) human follicular fluid (HFF) (the hyperactivation step). A CASA evaluation of hyperactivation will be performed. Swim-up capacitation and hyperactivation will be performed for all test substances. The HFF will be stripped of steroids and varying concentrations of progesterone will be added to examine the role of progesterone in inducing hyperactivation. Following the completion of the progesterone portion of the study, the effects of various compounds (calcium channel blockers, phospholipase A2 inhibitors, free fatty acids, and platelet activating factor) on hyperactivated motility will be evaluated. Depending on the type of data analyzed, either Chi-square or repeated measures ANOVA will be used for statistical analysis.

**Progress :** No subjects entered in FY 95.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 90/038		<b>Status:</b> On-going	
<b>Title:</b> Detailed Studies Into Membrane Lipid Synthesis in Human Sperm					
<b>Start Date:</b> 02/16/90			<b>Est. Completion Date:</b> Feb 99		
<b>Department:</b> Medicine, Endocrinology Svc			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL Robert E. Jones, MC					
<b>Associate Investigators:</b> CPT Brenda K. Bell, MC			Stephen R. Plymate, M.D.		
<b>Key Words:</b> lipid synthesis,human sperm					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$3494.00		04/05/91	

**Study Objective:** To elucidate the biochemical pathways for membrane lipid synthesis (excluding cholesterol) present in freshly ejaculated human spermatozoa from donors of proven fertility.

**Technical Approach:** Sperm will be washed and the sample diluted to achieve a concentration of  $2 \times 10^8$  sperm/ml. The incubation buffer, optimized for fatty acid activation, will consist of 380 mM TRIS [pH 8.4], 20 mM ATP, 20 mM  $MgCl_2$ , 0.1 mM coenzyme A (CoASH), 5 mM dithiothreitol, and 10-50 mM fatty acid, either 3H-9,10-16:0, 14C-1-16:0, or 14C-1-22:6. The reaction will be initiated by the addition of 107 sperm. Blank incubations will be performed in the absence of CoASH or the specific starting substrate to investigate the metabolic mechanisms of lipid turnover. Methylation of phosphatidylethanolamine (PE) will be measured by incubating 3H-methyl-S-adenosylmethionine (SAM) with diacyl PE or a 14C labeled fatty acid, 3H-SAM and 1-acyl-2-lyso PE. Another pathway for plasmalogen or ether lipid synthesis in nongerminal tissues will be assessed by incubating sperm with 14C-22:6, 1-palmitoyl-3-lyso PI (phosphatidylinositol) or -PC (phosphatidylcholine) and 3H-1-hexadecanol in the aforementioned buffer. Alternatively, 3H-hexadecanol, 14C-22:6, unlabeled 16:0 will be coincubated with dihydroxyacetone phosphate (DHAP). The reaction will be terminated after 1 hour and lipids will be extracted and dried. Incorporation of labeled fatty acids into sphingomyelin (SM) will be determined by detection of the fatty acyl radiolabel in the SM region of the thin layer chromatography (TLC) plates. After resolubilization in chloroform and methanol, lipids will be separated on LK5 TLC plates. Standards will be run on each plate and spots corresponding to standards will be scraped and counted. Plasmalogen formation will be assessed by performing mild acid hydrolysis on the extracted phospholipids prior to TLC or before rechromatography and determining DPM's in the fatty aldehyde and lysophospholipid regions. The presence of ether lipids will be determined by their resistance to alkaline and enzymatic hydrolysis prior to TLC. Mono and diacyl phospholipid synthesis will be assessed by free fatty acid release from SM and by using phospholipases A2 (PLA2) and B (PLB).

**Progress :** No subjects entered in FY 95. Manuscript in preparation.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 83/081		<b>Status:</b> Completed	
<b>Title:</b> Studies on Fatty Acid Activation in Spermatozoa[colon] Kinetics and Localization					
<b>Start Date:</b> 09/16/83			<b>Est. Completion Date:</b> Sep 84		
<b>Department:</b> Medicine, Endocrinology Svc			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL Robert E. Jones, MC					
<b>Associate Investigators:</b> COL Bruce L. Fariss, MC			Stephen R. Plymate, M.D.		
<b>Key Words:</b> spermatozoa,fatty acid					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$785.00		04/05/91	

**Study Objective:** To define the kinetic characteristics and cellular localization of the enzyme system responsible for the initiation of saturated fatty acid metabolism in spermatozoa.

**Technical Approach:** Normal human semen samples will be used to establish a ligase assay. Ligase activity will be measured using a sensitive radioligand/millipore filter procedure that utilizes (3H)-coenzyme A as the radioactive trace. Approximately 0.2 mC of (3H) will be present in each individual assay. The samples will be centrifuged at 2800g for 10 minutes at room temperature, the seminal plasma supernatant will be discarded, and the sperm pellet will be resuspended in an isotonic buffer. This sperm mixture will be recentrifuged and washed twice prior to use. After the final centrifugation, the pellet will be diluted in a potassium enriched buffer to achieve a sperm density of  $2 \times 10^8$ /ml. The assay mixture will contain palmitic acid, ATP,  $Mg^{++}$  and CoASH and will be initiated by the addition of the washed sperm preparation. Time and protein dependency curves will be run to determine the length of incubation needed to achieve first order kinetics in the measurement of initial velocities. Both Lineweaver-Burk plots and hyperbolic best-fit will be used to calculate approximate  $K_m$  values for each substrate. Temperature, pH curves, and rates with alternate substrates will also be run. Enzyme location/latency will be determined by assaying separate cell fractions prepared by sonication and differential centrifugation of the isolated sperm. The effects of sulfhydryl reagents, albumin, and detergents will be studied to assist in estimation of latency.

**Progress :** No further work was performed this FY. Published article in J Andrology in Dec 1994.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 88/026	<b>Status:</b> Completed
<b>Title:</b> Neutral and Polar Lipid Synthesis in Human Spermatozoa[colon] A Correlation with Morphology and Function		
<b>Start Date:</b> 01/15/88	<b>Est. Completion Date:</b> Jun 89	
<b>Department:</b> Medicine, Endocrinology Svc	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> COL Robert E. Jones, MC		
<b>Associate Investigators:</b> MAJ Karl E. Friedl, MC		Stephen R. Plymate, M.D. MAJ Charles J. Hannan, MC
<b>Key Words:</b> spermatozoa, lipids, morphology		
<b>Accumulative MEDCASE Cost:</b> \$40000.00	<b>Est. Accumulative OMA Cost:</b> \$2000.00	<b>Periodic Review:</b> 04/05/91

Study Objective: To compare the rates of fatty acid activation to acyl CoA and subsequent disposal into neutral or polar lipids with sperm morphology or an assessment of sperm motility.

Technical Approach: The incorporation of palmitic (16:0) and docosahexaenoic acids (22:6) into neutral or phospholipids will be measured by incubating whole, fresh sperm with 3H-16:0 and 14C-22:6. Total lipids will be extracted using the method of Bligh and Dyer. The chloroform phase will be taken to dryness under N<sub>2</sub> at 42°C and subsequently reconstituted in a minimal volume of chloroform. The chloroform mixture will be applied to a silicic acid column and subsequently eluted with 20 ml chloroform followed by 20 ml of methanol. The chloroform fractions containing neutral lipids will be combined, evaporated, and repeatedly extracted to remove the free fatty acids. Both the methanol and chloroform elutes will be counted, and an aliquot of each will be chromatographed on silica gel G to ensure complete separation. Incorporation rates will be expressed as nmoles fatty acid incorporated/10<sup>6</sup> sperm or nmoles phospholipid P/hour. After extracting the sperm with 0.1% Triton X100, ligase activity will be measured. Both 16:0 and 22:6 will be used as substrates in the incubations. Ligase activity will be expressed as nmoles acyl CoA formed/min/mg protein. The seminal plasma concentrations of these compounds will be measured using an enzymatic spectrophotometric technique. These parameters will be considered separately in relationship to ligase activity and lipid synthesis. Semen samples will be handled and analyzed according to the current WHO guidelines. Morphology will be assessed on fixed smears, and motility will be objectively quantified with an automated semen analyzer. With the exception of the sperm density, the semen quality will be blinded to the person performing the biochemical analyses. Incorporation rates and the distribution of the fatty acid labels and ligase activity will be correlated with sperm morphology and motility of the semen sample using either linear regression or chi-square analyses.

Progress : No subjects studied in FY 95.

## Detail Summary Sheet

**Date:** 30 Sep 95      **Protocol No.:** 92/068      **Status:** Completed

**Title:** The Time Course for Metabolic Responses to Thyroid Hormone[colon] Specific Contributions of Muscle Efficiency and Resting Oxygen Utilization

**Start Date:** 06/05/92

**Est. Completion Date:** Jan 94

**Department:** Medicine, Endocrinology  
Svc

**Facility:** MAMC

**Principal Investigator:** LTC Homer J. Lemar Jr., MC

**Associate Investigators:**  
COL Robert E. Jones, MC  
LTC H. Lester Reed, MC

COL David L. Bunner, MC  
CPT Carl A. Gibson, MC

**Key Words:** thyroid hormone, muscle efficiency, oxyten utilization

Accumulative	Est. Accumulative	Periodic Review:
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	//

**Study Objective:** To determine the relationship between serum thyrotropin (TSH) concentrations and the efficiency of skeletal muscle during a changing thyroid status; to identify if these measures of pituitary and peripheral thyroid hormone action covary with the same time constant in transition from hyperthyroidism to euthyroidism; and to assess the specific contribution of a changing muscle work efficiency to the increased oxygen utilization associated with excess states of thyroid hormone.

**Technical Approach:** Oxygen utilization will be measured with four submaximal bicycle ergometer workloads in 15 hyperthyroid patients undergoing treatment and 15 euthyroid control subjects. These workloads will support a linear regression analysis to determine muscle efficiency and resting oxygen use. This measure will be carried out before and biweekly during treatment for hyperthyroidism in order to determine the time course of tissue responses during normalization of serum thyroid hormones. Specifically, serum thyrotropin (TSH) will be simultaneously measured and the time course of normalizing sensitive assays of serum TSH and exercise kinetics will be contrasted as two tissue responses to this changing thyroid hormone status. Euthyroid controls will establish normal ranges and the test variability, while allowing comparisons between themselves and the hyperthyroid and hypothyroid subjects. The study population will include hyperthyroid patients who have elected radioactive iodine therapy for their disease and a control group of normal euthyroid patients who are taking a stable and fixed replacement dose of thyroid hormone.

**Progress :** 6 treated Graves and 6 controls entered study. The metabolic effects of acute HYPO appear to be mild.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 93/127	<b>Status:</b> Completed
<b>Title:</b> Oncogene Activation in Neoplastic Thyroid Tissue Occurring After Exposure To A Nuclear Blast[colon] The Marshall Island Experience		
<b>Start Date:</b> 06/09/93	<b>Est. Completion Date:</b> Jun 94	
<b>Department:</b> Medicine, Endocrinology Svc	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Robert M. Tuttle, MC		
<b>Associate Investigators:</b>		
Sissy S. Jhiang, Ph.D.	COL Ernest L. Mazzaferri, MC	
CPT Rodger K. Martin, MS	MAJ Robert B. Ellis, MC	
Michael Bourneman, MC	MAJ Richard R. Gomez, MC	
Jean Howard, M.D.	Larry Sakas, MC	
	Goerge Begus, M.D.	
<b>Key Words:</b> thyroid, nuclear blast, oncogene activation		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$3174.00	//

**Study Objective:** 1. To determine the frequency of activation of the Papillary Thyroid Cancer (PCT/retTPC) oncogene in neoplastic thyroid tissue that developed after exposure to a nuclear blast. 2. To determine the frequency of K-ras point mutations in neoplastic thyroid tissue that developed after exposure to a nuclear blast. 3. To correlate the clinical course of these radiation induced thyroid cancers with the activation of each oncogene.

**Technical Approach:** Approximately 30 samples of paraffin embedded thyroidectomy samples from individuals with a documented presence in the Marshall Islands in 1954 and with a diagnosis of papillary thyroid cancer, follicular thyroid cancer, or other non-malignant neoplasia and any normal thyroid tissue available will be used to recover DNA and mRNA using techniques that have proven successful in our laboratory. These samples will be compared with samples from (1) Marshall Islanders not exposed to fallout that developed thyroid neoplasia (2) non-radiation induced thyroid neoplasia collected at Ohio State University (OSU) and Madigan Army Medical Center (MAMC). The paraffin blocks will be sectioned on a microtome using sterile technique and a new microtome blade for each block. A new histology slide will be prepared and reviewed to verify that thyroid tissue is present in the block and to re-confirm the diagnosis. The paraffin sections will be placed into a sterile 1.5 ml sterile microcentrifuge tube and sealed. A sample from each paraffin block will be blindly evaluated by both the laboratory at OSU and MAMC. The DNA and messenger RNA extracted from the paraffin embedded tissue will be examined to determine quality and quantity of extracts. Optical densities (OD 260/280) and agarose mini-gel electrophoresis will be done on sample extracts. Beta-2 microglobulin and the TSH receptor will be amplified with PCR to document integrity of the nucleic acids recovered. Samples in which the constitutively expressed messenger RNA's can be amplified with PCR will be used for oncogene amplification. The mRNA extract will serve as substrate for cDNA synthesis using the specific PTC downstream primer. The cDNA will then serve as substrate for PCR. After PCR, the mixture of amplified products generated from a specific primer set will be separated by size using standard agarose gel electrophoresis. Appropriate size markers will be used to provide size

parameters of amplified products. Additional characterization of the PCR amplified product includes Southern hybridization studies with specific DNA oligomer probes. The oligonucleotide probes will be 3 prime tailing with digoxigenin dUTP or 5 prime labelled with  $^{32}\text{P}$ . Chemilluminescent detection will be done using the Genius/Lumiphos detection method. This method has been used successfully in our lab to detect picomolar amounts of target DNA.

Statistically, the rates of activation of each oncogene in each subgroup will be compared using chi-square testing. Unpaired t test and Fischer's exact test will be used to determine if oncogene activation is more frequent in metastatic disease versus non-metastatic disease and to compare baseline measurements between groups. Logistic regression analysis of those clinical variables shown to be significant by chi-square will be used to determine which single or combination of variables correlate with oncogene activation. Finally, to determine whether the activation of the oncogene is a significant prognostic factor, univariate and multivariate Cox regression will be used defining failure as first recurrence or never disease free and assuming the oncogene activation was present at diagnosis.

Progress : 122 subjects entered. Transferred to WRAMC and just started data analysis.



**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF MEDICINE, GASTROENTEROLOGY**  
**SERVICE**

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/182	<b>Status:</b> On-going
<b>Title:</b> Evaluation of the Performance of Fecal Occult Blood Tests in High Risk Patients Undergoing Colonoscopy		
<b>Start Date:</b> 08/18/95	<b>Est. Completion Date:</b>	
<b>Department:</b> Medicine, Gastroenterology Svc	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Robert H. Sudduth, MC		
<b>Associate Investigators:</b> D.C. Sadowski L. Bertario M. Epstein	P. Rozen R. Gnauck D.C. Rockey G. Zuckerman	
<b>Key Words:</b> occult blood, FlexSure, HemeSelect, Hemoccult, Hemoccult SENS		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objectives:** The primary objective of this study is to compare the sensitivity of the different fecal occult blood tests (FOBTs) for the detection of colorectal neoplasia in a high risk population. The data collected will support regulatory submissions for the FlexSure<sup>R</sup> OBT (FS) in the USA.

**Technical Approach:** This is a multi-center study involving private and institutional gastroenterology practices. 250 colonoscopy patients who meet the inclusion criteria will be recruited to participate. Using established mechanisms that may be unique for each study center, patients will be asked to collect samples from three consecutive bowel movements while observing certain dietary and drug restrictions (no red meat, high peroxidase-containing vegetables, vitamin C, aspirin and non-steroidal anti-inflammatory drugs). Generally, stool collections will be done prior to colonoscopy, except as noted in the inclusion criteria. After consenting, patients will be provided a FOBT kit. The kit will have all the necessary materials and instructions for collecting their stool samples. The completed kits are then returned to a designated site or laboratory at the study center. All FOBTs will be developed at the study center except for HemeSelect<sup>R</sup>. Results of FOBTs and clinical findings will be reviewed and correlated. The test positivity rate on patients confirmed to have colorectal neoplasia (colorectal cancer and adenomas  $\geq 1$ cm) will be the measurement of the test sensitivity. The negative predictive values for each of the tests will also be compared.

**Progress :** Protocol is awaiting approval from CIRO.

## Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 94/086

**Status:** On-going

**Title:** The Location of the Esophageal Lesion Responsible for Dysphagia. How Accurate is the Patient's History?

**Start Date:** 04/01/94

**Est. Completion Date:** Jan 94

**Department:** Medicine, Gastroenterology  
Svc

**Facility:** MAMC

**Principal Investigator:** MAJ Amy M. Tsuchida, MC

**Associate Investigators:**  
CPT Eric T. Fajardo, MC  
LTC Gregory N. Bender, MC

MAJ Michael F. Lyons II, MC  
CPT Thomas P. Peller, MC

**Key Words:** dysphagia, esophageal lesion

**Accumulative**

**MEDCASE Cost:** \$0.00

**Est. Accumulative**

**OMA Cost:** \$31.65

**Periodic Review:**

//

**Study Objective:** To correlate the patient's localization of the site of food impaction with the site of the lesion by endoscope and barium swallow.

**Technical Approach:** The patients entered into this study will receive a directed history and physical exam as well as a CBC and thyroid function test. As part of the history, the patients will be asked to fill out a questionnaire on which foods they can swallow easily. Each food will be given a numeric value as follows: soup (1), mashed potatoes (2), peas (3), peeled apple (4), meat (5), wholemeal bread (6). A dysphagia score of 0-20 will then be established. After this initial exam the patients will receive an esophagogastroduodenoscopy (EGD) and barium swallow study per standard gastroenterology and radiology protocols. The physicians participating in the study will be blinded to the results of previous tests. The patients will be educated to the risks and benefits of the procedures and informed consent will be obtained. At the time of the procedure the patient will be asked to localize the site where food sticks or hangs up. A radiographic marker will then be placed over this/these point(s). Endoscopy and barium swallow will then be performed in the standard fashion. The site of the culprit esophageal lesion will be documented roentgenographically. We will compare the site of the lesion on the x-ray with the nipple marker. A correct localization will be defined as the nipple marker lying within two centimeters of the lesion on x-ray. Data will be analyzed descriptively by comparing the site of lesions on endoscopy and swallowing study with the external x-ray markers.

**Progress :** 21 subjects have been entered, 9 of whom were found to have no endoscopically apparent lesions. 5 of these reported the level of dysphagia at the suprasternal notch, 2 in the mid chest and 2 at the level of the xiphoid process. There was a wide variation in the level of subjective dysphagia. Subject accrual continues.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/067		<b>Status:</b> On-going	
<b>Title:</b> A Study to Evaluate the Effects of Therapy with Lansoprazole and Clarithromycin and/or Amoxicillin on the Eradication of Helicobacter pylori and the Recurrence of Duodenal Ulcer					
<b>Start Date:</b> 02/17/95			<b>Est. Completion Date:</b> Mar 96		
<b>Department:</b> Medicine,Gastoenterology Svc			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Amy M. Tsuchida, MC					
<b>Associate Investigators:</b> MAJ Kazunori Yamamoto, MC			MAJ Robert H. Sudduth, MC MAJ John G. Carrouger, MC		
<b>Key Words:</b> ulcer:duodenal, Helicobacter pylori, Lansoprazole, Clarithromycin, Amoxicillin					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
<b>Periodic Review:</b>					//

**Study Objective :** This Phase III study is designed to compare the safety and efficacy of monotherapy with lansoprazole, dual therapy with lansoprazole and amoxicillin or lansoprazole and clarithromycin, and triple therapy with lansoprazole, clarithromycin and amoxicillin for the eradication of *Helicobacter pylori* from the gastric mucosa of patients with active duodenal ulcer or a history of duodenal ulcer. This study also allows the comparison of duodenal ulcer prevalence rates after treatment for the eradication of *H. pylori* with the aforementioned therapies.

**Technical Approach :** This Phase III randomized, double-blind, parallel-group, active-controlled study will compare the effectiveness of two dual therapy regimens of lansoprazole and clarithromycin, two dual therapy regimens of lansoprazole and amoxicillin, and one triple therapy regimen of lansoprazole, clarithromycin, and amoxicillin to monotherapy with lansoprazole 30 mg TID. Approximately 45 study sites will provide a total of 390 patients. At each site, patients will be stratified by baseline DU status (active or healed) and within each stratum randomly assigned in an equal ratio such that 65 patients will be assigned to each the six treatment groups. Patients with duodenal ulcer (DU) or a history of DU endoscopically proven within the past year will have a blood sample taken to determine the presence of antibodies to *H. pylori*. Patients with a positive result will undergo an endoscopy within seven days prior to initiating study treatment. At this screening endoscopy, the duodenal ulcer(s), if present, will be documented, gastric biopsy specimens will be taken from the antrum and the body of the stomach for culture and histology of *H. pylori*, and an additional biopsy specimen will be taken from the greater curvature of the antrum for the rapid urease test (i.e., CLOtest). Patients will also undergo a complete physical examination and a clinical laboratory evaluation at this visit. If a patient is positive for *H. pylori* by rapid urease test, the patient may be considered for entry into the study. If a patient is negative for *H. pylori* by rapid urease test but is subsequently determined to be *H. pylori* positive by histology, the patient will be considered *H. pylori* positive and may qualify for entry into the study.

All patients meeting the selection criteria listed in Section 5.0 (Selection of Patients) will be dispensed study medication and patient diaries on Baseline Day 1. Study medication will be stratified according to a patient's baseline DU status (active

or healed). Gelusils will be provided for relief of symptoms.

Patients will self administer study medication for the next 14 days. Patients will receive therapy for 14 consecutive days. Patients will return to the study center at Week 2 for a brief evaluation and collection of all study medication containers. Additional Gelusil may be dispensed at the Week 2 visit, if needed.

Patients will return at Week 6 (four weeks post-treatment) for an evaluation which will include endoscopy, with the collection of gastric biopsies for culture and histology of *H. pylori*.

All patients completing the Week 6 visit with healed DU will return to the study center for evaluation at three and six months after completion of active treatment. Patients may test either positive or negative for *H. pylori* at the Week 6 visit, but must be free of active duodenal ulcer to continue in the post-treatment period. The three and six month evaluations will include physical examinations, clinical laboratory evaluations, and endoscopy to determine the presence of duodenal ulcer (including collection of gastric biopsy specimens for culture and histology of *H. pylori*).

Gelusil will be provided for relief of symptoms and will be the only antiulcer medication permitted during the post-treatment period. Patients will be instructed to use Gelusil on an as-needed basis only. No other study medication will be administered to patients during the post-treatment period.

Progress : One subject has been entered and subject accrual continues.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF MEDICINE,**  
**HEMATOLOGY/ONCOLOGY SERVICE**

## Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 95/069

**Status:** Completed

**Title:** Risk Assessment Technical Policy for Conduct of Clinical Research  
Project[colon] Subject Interview Study

**Start Date:** 02/17/95

**Est. Completion Date:** Mar 95

**Department:** Medicine,  
Hematology/Oncology Service

**Facility:** MAMC

**Principal Investigator:** MAJ Kenneth A. Bertram, MC

**Associate Investigators:**  
MAJ Steven S. Wilson, MC

MAJ Patrick A. Cambier, MC

**Key Words:** risk assessment, clinical research

**Accumulative**

**Est. Accumulative**

**Periodic Review:**

**MEDCASE Cost:** \$0.00

**OMA Cost:** \$0.00

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**Study Objective:** The primary objective of this study is to identify issues and common themes related to the conduct of research involving human subjects, with a focus on research subject recruitment, informed consent, and respondents' understanding and experience of the research process. The information will be used by the Advisory Committee on Human Radiation Experiments to help inform the development of recommendations and future policies and practices related to human radiation research.

**Technical Approach:** The study is an empirical investigation of individuals' experiences, beliefs and attitudes about research involving human subjects. The study will sample research participants and non-participants at 15 institutions across 4 sites.

To permit useful comparisons between groups of patients whose medical care involves the therapeutic and/or diagnostic use(s) of radiation and those whose care does not involve radiation, patients from medical oncology, radiation oncology, and cardiology will be recruited for interviews. Brief (5-10 minutes), structured interviews will be conducted with 2,250 respondents (50 from each of the 3 clinics for a total of 150 patients from each institution). A longer (30-45 minutes), indepth interview will be conducted with a subsample of 125 respondents. No more than 10 in-depth interviews will be conducted at each institution.

Cross-tabulations will be generated by institution type, research participant versus non-participant status, respondent sociodemographic and other variables to determine whether cell sizes are sufficient to identifying potential correlates and distinct response pattern differences among key respondent subgroups. Response categories reflecting attitudes toward research and reasons for participating in research will be developed for use in analyzing questions such as whether or not there are gender, age, ethnic, or socioeconomic differences associated with particular attitudes and reasons for participating. Likewise, additional analytic questions will be addressed concerning subgroup differences (e.g., sociodemographic characteristics, perceived illness severity, medical specialty, extent of information given) in perceived advantages and disadvantages of participating in research, perceptions of press and coercion, etc. Another respondent group of particular analytic interest for the study are the research non-participants and their attitudes and perceptions of research, research participation, expressed willingness to participate, and concerns about participation. Data from the in-depth interviews (audiotaped) will be analyzed using a qualitative analysis software package (TALLY).

**Progress :** 60 patients were enrolled. This protocol was part of a national project. No final results have been released to MAMC's Principal Investigator at this time.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/057		<b>Status:</b> On-going	
<b>Title:</b> A Randomized, Double-Blind, Acyclovir-Controlled, Multicenter Study to Assess the Safety, Efficacy, and Pharmacokinetics of IV Penciclovir for the Treatment of Mucocutaneous Herpes Simplex Infection..					
<b>Start Date:</b> 02/04/94			<b>Est. Completion Date:</b> Feb 95		
<b>Department:</b> Medicine, Hemotology/Oncology Service			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Kenneth A. Bertram, MC					
<b>Associate Investigators:</b>			CPT John R. Caton, MC		
<b>Key Words:</b> herpes simplex, immunocompromised, penciclovir, intravenous					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		//	

**Study Objective:** To compare the safety and efficacy of intravenous penciclovir, at a dose of 5 mg/kg 2-3 times daily for 7 days, with 5 mg/kg intravenous acyclovir 3 times daily for 7 days in the treatment of mucocutaneous herpes simplex infection in immunocompromised patients.

To study the population pharmacokinetics of intravenous penciclovir at a dose of 5 mg/kg 2 and 3 times daily in immunocompromised patients with mucocutaneous herpes simplex infection.

**Technical Approach:** This is a randomized, three dose arm, parallel-group, multicenter study. Double-blind treatment will be allocated sequentially by means of a fixed, equally balanced randomization code by the pharmacist. Patients at least eighteen years of age with a clinical mucocutaneous herpes simplex infection and are immunocompromised will receive intravenous penciclovir, at a dose of 5 mg/kg either two or three times daily for 7 day, will be compared with intravenous acyclovir at a dose of 5 mg/kg three times daily for 7 days.

Patients will be evaluated daily during the 7 day treatment period and thereafter every other day until complete healing (re-epithelialization of lesions) has occurred, for clinical signs and symptoms, assessment of herpetic lesions and viral culturing. Laboratory tests will be conducted at baseline, at the end of the treatment period and one week after the treatment period. Four blood samples for population pharmacokinetic studies will be taken on one of the full treatment days only.

Data collected from the study will be evaluated by the sponsor.

**Progress :** No patients enrolled in FY95. Protocol recently approved by DA and remains on-going for patient enrollment.



### Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 94/070

**Status:** Completed

**Title:** A Dose Ranging, Efficacy, Safety, and Pharmacokinetic Study of Single Oral Doses of RS-25259 for Prevention of Nausea and Vomiting in Chemotherapy-Naive Cancer Patients Receiving Highly Emetogenic ...

**Start Date:** 03/04/94

**Est. Completion Date:** Aug 95

**Department:** Medicine,  
Hematology/Oncology Service

**Facility:** MAMC

**Principal Investigator:** MAJ Kenneth A. Bertram, MC

**Associate Investigators:**

LTC Howard Davidson, MC

**Key Words:** antiemetic:RS-25259, chemotherapy, cancer

**Accumulative**

**MEDCASE Cost:** \$0.00

**Est. Accumulative**

**OMA Cost:** \$0.00

**Periodic Review:**

10/21/94

**Study Objective:** 1.) To determine the dose-response relationship among single oral doses of RS-25259 over the dose range of 3-30 mcg/kg. 2.) To assess the safety of single oral doses of RS-25259 administered through the range of doses tested in this patient population. 3.) To assess the pharmacokinetics of single oral doses of RS-25259 through the range of doses tested in this patient population.;

**Technical Approach:** Patients 18 years of age and older with a proven diagnosis of cancer who are chemotherapy-naive will be invited to participate in this study. After informed consent is obtained they will give a full medical history and undergo a full physical exam including a 12-lead ECG, and submit blood and urine for laboratory examination.

On Dosing Day, patients will be assigned a patient number. At -90 minutes (1 1/2 hours before the start of chemotherapy) the patient will have sitting blood pressure and heart rate recorded and complete the predose nausea assessment. At -60 minutes, RS-25259 will be given orally. Sitting blood pressure and heart rate will be recorded again at -20 minutes, then at 30 minutes, 1.5, 3.5, 7.5, and 23.5 hours after the commencement of chemotherapy. At 24 hours a limited physical and 12-lead ECG will be done.

Diary cards will be provided to record the number of emetic episodes and to record the degree of nausea at various timepoints. At follow-up, 2 week after dosing, patients will have a limited physical, and submit blood and urine samples for laboratory evaluation. 12-lead ECG will be repeated for those patients who had an abnormal ECG at 24 hours. At 14 days patients will be contacted either by telephone or during a visit and questioned regarding adverse events and concomitant medications.

**Progress :** 10 patients were enrolled. One patient died following completion of the study; his death was determined to be unrelated to the study drug. The protocol closed to patient accrual 20 March 95, however the 9 remaining patients continue to be followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/080		<b>Status:</b> On-going	
<b>Title:</b> Letrozole (CGS 20267) Comparison of Two Doses (0.5 mg and 2.5 mg) of Letrozole versus Megestrol Acetate in Postmenopausal Women With Advanced Breast Cancer, Protocol 02					
<b>Start Date:</b> 04/01/94			<b>Est. Completion Date:</b> Oct 99		
<b>Department:</b> Medicine, Hemotology/Oncology Service			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Kenneth A. Bertram, MC					
<b>Associate Investigators:</b>			LTC Howard Davidson, MC		
CPT John R. Caton, MC			James H. Timmons, MD		
MAJ Timothy P. Rearden, MC			LTC Luke M. Stapleton, MC		
MAJ Robert B. Ellis, MC			LTC Robert D. Vallion, MC		
CPT Diana S. Willadsen, MC			CPT James S. D. Hu, MC		
MAJ Richard F. Williams, MC					
<b>Key Words:</b> Cancer:breast, Letrozole, megestrol acetate, postmenopausal					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	10/21/94	

**Study Objective:** 1) To compare the anti-tumor efficacy, as evaluated by the primary variable of objective response rate, and the secondary variables of duration of response, time to treatment failure (TTF), time to progression (TTP) and time to death among the three treatment arms (daily) doses of 0.5 mg letrozole, 2.5 mg letrozole, or 50 mg megestrol acetate (q.i.d.). 2) To compare tolerability and toxicity of daily doses of 0.5 mg letrozole, 2.5 mg letrozole and 40 mg megestrol acetate q.i.d. 3) To assess information on population pharmacokinetics, including evaluation of trough estrogen levels during treatment, with daily doses of 0.5 mg and 2.5 mg letrozole.

**Technical Approach:** This is a multicenter, multinational, randomized, parallel-group, double-blind trial in postmenopausal women with advanced breast cancer who have failed on antiestrogen as an adjuvant or advanced disease therapy. Patients will receive either one tablet letrozole 0.5 mg or 2.5 mg once daily in the morning plus one placebo capsule matching megestrol acetate q.i.d. or one 40 mg capsule megestrol acetate q.i.d. plus one placebo tablet matching letrozole once daily in the morning. Patient evaluations will be done at baseline (prior to treatment), after 2 weeks, 1, 2, 3, 4, 5 and 6 months and every 3 months thereafter until the code is broken to the participating investigators which will occur after the last patient has been enrolled for 18 months. In addition any patient who manifests an objective tumor response will have her full tumor evaluations repeated at least 4 weeks but no later than the next scheduled tumor assessment after the initial observation of response to confirm the presence of the response. Patients who respond to treatment (complete response, partial response or stable disease) will continue the treatment until the double-blind code is broken or there is disease progression, whichever comes first. After this period, the patients will be followed periodically for the purpose of collecting survival data for a total period of 5 years after initiation of treatment of the first patient on trial.

**Progress :** 2 patients were enrolled. Both patients showed progressive disease while on study treatment and were withdrawn from the study. Patient accrual continues.

## Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 94/017

**Status:** On-going

**Title:** Evaluation of Immunity to Breast Cancer

**Start Date:** 02/04/94

**Est. Completion Date:** Nov 94

**Department:** Medicine,  
Hematology/Oncology Service

**Facility:** MAMC

**Principal Investigator:** MAJ Kenneth A. Bertram, MC

**Associate Investigators:**

LTC Howard Davidson, MC  
MAJ Robert B. Ellis, MC  
CPT James S. D. Hu, MC  
CPT Diana S. Willadsen, MC  
CPT John R. Caton, MC

LTC Luke M. Stapleton, MC  
MAJ Patrick L. Gomez, MC  
MAJ Richard C. Tenglin, MC  
LTC Robert D. Vallion, MC  
MAJ Mark E. Robson, MC  
MAJ Richard F. Williams, MC

**Key Words:** cancer:breast, immunity

**Accumulative**

**MEDCASE Cost:** \$0.00

**Est. Accumulative**

**OMA Cost:** \$18.00

**Periodic Review:**

//

**Study Objective:** To determine the significance/relationship of CD4 helper/inducer T cell response in the presence of H2N positive/negative cancers in an attempt to determine how the immune system responds to breast cancer.

**Technical Approach:** Patients with breast cancer will have samples of tumor tissue obtained at the time of surgery for Her-2/neu. Blood will be obtained at the same time to evaluate for an anti-Her-2/neu T-lymphocyte response. Further venipunctures will be performed monthly during the 5 year follow-up period to continue evaluation for an anti-Her-2/neu T-lymphocyte response.

**Progress :** 40 subjects have been enrolled. 5 had a response to HER2/neu protein. Continue to look at original tumor cells to see if it expresses the specific target antigen.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/099	<b>Status:</b> On-going
<b>Title:</b> Phase III Trial of 3-Hour versus 96-Hour Infusions of Paclitaxel from NaPro/Baker Norton in Patients with Refractory Metastatic Breast Cancer, and an Assessment of 96-Hour Infusions in 3-Hour Failures		
<b>Start Date:</b> 03/17/95	<b>Est. Completion Date:</b> Nov 96	
<b>Department:</b> Medicine, Hematology/Oncology Service	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Kenneth A. Bertram, MC		
<b>Associate Investigators:</b>		
MAJ Robert B. Ellis, MC	LTC Luke M. Stapleton, MC	
LTC Robert D. Vallion, MC	CPT James S. D. Hu, MC	
CPT Diana S. Willadsen, MC	MAJ Richard F. Williams, MC	
<b>Key Words:</b> Cancer:breast, paclitaxel		
<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	//

**Study Objectives:** Primary: To confirm the established therapeutic effects of paclitaxel in refractory metastatic breast cancer patients given the approved dose and schedule of a new source of this novel chemotherapeutic agent. Secondary: To confirm the safety profile and patient tolerance characteristics of paclitaxel under the widely accepted therapeutic regimen, to offer a new regimen of paclitaxel (by 96-hour infusion) as a rescue therapy for patients progressing on the standard paclitaxel regimen, and to confirm the reported higher efficacy of the 96-hour infusion regimen of paclitaxel in a subset of patients selected randomly de novo.

**Technical Approach:** This investigation is a multi-center, open-label, Phase II/III, trial evaluating 3-hour and 96-hour infusions of paclitaxel from NaPro/Baker Norton. The study population is women with metastatic breast cancer who have failed a maximum of two prior chemotherapy regimens, only one of which may have been as treatment for metastatic disease. The study will enroll 200 patients, approximately 75% of whom are expected to have been exposed to anthracyclines. Patients will be stratified on the basis of measurable versus evaluable disease. Patients will be randomized to the 3-hour and 96-hour infusions in each strata on a 3 to 1 ratio. Patients randomized to the treatment group using the 3-hour schedule will crossover to the 96-hour schedule when there is evidence of rapid progression. Rapid progression is defined as increase of disease within a maximum of 4 cycles of 3-hour paclitaxel infusion. Estimation of the response rate to a 3-hour infusion will be determined in 150 patients. The second objective of obtaining estimates of the response rate to a 96-hour infusion will be obtained in an additional 50 patients. The assignment of patients to infusion schedules will be done by randomization. Response rates of 26% and 48% have been reported for the 3-hour and the 96-hour schedules. The 95% confidence limits for these infusion rates are less than 7.8% for the 3-hour and less than 14.4% for the 96-hour rate, and are the basis for sample sizes of 150 and 50 patients, respectively.

**Progress :** No patients were enrolled in FY95. Patient accrual continues.

### Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 95/162

**Status:** On-going

**Title:** The Characterization of Breast Cancer Susceptibility Genes in Males and Their Kindred

**Start Date:** 08/18/95

**Est. Completion Date:** Sep 98

**Department:** Medicine,  
Hematology/Oncology Service

**Facility:** MAMC

**Principal Investigator:** CPT John R. Caton, MC

**Associate Investigators:**  
A. Langston

MAJ Robert B. Ellis, MC  
E. Ostrander

**Key Words:** cancer:breast, gene:BRCA1, gene:BRCA2, AT, gene:p53,  
gene:retinoblastoma, ras

**Accumulative**

**MEDCASE Cost:** \$0.00

**Est. Accumulative**

**OMA Cost:** \$0.00

**Periodic Review:**

//

**Study Objective:** Using male breast cancer patients as probands we will characterize the known breast cancer susceptibility genes BRCA1, BRCA2, AT and additional genes such as p53, RB and ras in the affected individuals and their families.

**Technical Approach:** The data obtained from a previous study of the Automated Central Tumor Registry database (ACTUR) revealed 123 total cases of male breast cancer within the Department of Defense (DOD) healthcare system. Those patients with a family history of breast cancer are currently in the process of evaluation under a previous IRB approved protocol. The next step involves collecting samples of blood from each living male breast cancer patient and family members of both living and deceased patients as deemed appropriate for study. Additionally, formalin fixed paraffin imbedded tumor blocks will be collected on as many patients as possible. Once the specimens are collected the blood will be processed at Madigan Army Medical Center. Both DNA and buffy coat cells will be extracted and frozen for storage. Aliquots of these specimens along with portions of tumor blocks will be blinded with regard to clinical information and sent to Dr. Ostrander's lab at Fred Hutchinson Cancer Research Center for analysis. This analysis will initially include screening for mutations in BRCA1, BRCA2 (when cloned) and the Ataxia-Telangiectasia gene (AT) using the patient DNA extracted from the blood sample. The tumor blocks would be tested for the loss of heterozygosity for markers on chromosomes 13q covering both the BRCA2 and Retinoblastoma (RB) genes, chromosome 11 for the AT gene and chromosome 17 regions covering the p53 and BRCA1 genes. Data collected from these studies would then be matched with the clinical information in order to derive information regarding cancer susceptibility, prognosis and basic mechanisms of carcinogenesis.

**Progress :** 72 subjects entered. Funding won't be available til 1 Jan 1996, the study can then be completed.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/118	<b>Status:</b> On-going
<b>Title:</b> The Natural History of Male Breast Cancer		
<b>Start Date:</b> 04/21/95	<b>Est. Completion Date:</b> Apr 95	
<b>Department:</b> Medicine, Hemotology/Oncology Service	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT John R. Caton, MC		
<b>Associate Investigators:</b> MAJ Timothy P. Rearden, MC                      MAJ Robert B. Ellis, MC		
<b>Key Words:</b> cancer:male breast, cancer:natural history		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objective:** To establish a comprehensive, complete database of information on male breast cancer patients diagnosed and treated in the Department of Defense.

**Technical Approach:** The Automated Central Tumor Registry (ACTUR) for the Department of Defense contains information on all cancer cases. This database was previously searched and 123 individuals with male breast cancer identified. Unfortunately, the database contains very little information other than names and addresses. A survey has been constructed for the patients to complete and will yield large amounts of information concerning epidemiology, natural history hereditary patterns, and treatment. The data will also be the foundation for other studies on the molecular basis of male breast cancer and comparison to female tumors.

**Progress :** 188 subjects entered. A major finding was that the patients from this series who were node positive had a much better overall survival rate than that previously reported. This was attributed to the aggressive adjuvant therapy that these subjects received. Another finding our series demonstrated was that the drug Tamoxifen was well tolerated which contrasted to a previous report from New York. The data collected on family histories in these patients has been the basis for grant applications for funding from DOD and American Cancer Society.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/049		<b>Status:</b> On-going	
<b>Title:</b> A Stratified, Randomized, Double-Blind Comparison of Oral Ondansetron and Compazine Spansules in the Prevention of Nausea and Vomiting Associated with Moderately Emetogenic Chemotherapy					
<b>Start Date:</b> 12/16/94			<b>Est. Completion Date:</b> Aug 95		
<b>Department:</b> Medicine, Hemotology/Oncology Service			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Robert B. Ellis, MC					
<b>Associate Investigators:</b> LTC Howard Davidson, MC			MAJ Kenneth A. Bertram, MC MAJ Richard F. Williams, MC		
<b>Key Words:</b> ondansetron, compazine spansules, chemotherapy					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> //

**Study Objective:** To compare the efficacy and safety of 8mg oral ondansetron BID with 15mg Compazine Spansules BID in the prevention of nausea and vomiting associated with a cyclophosphamide-based chemotherapy regimen. This study will also assess the impact of nausea, vomiting, and sleepiness on the productivity and activity levels of the subject population. The quality of life related to cancer and emesis will be compared between the two treatment groups.

**Technical Approach:** This will be a stratified, randomized, double-blind, multicenter, comparative trial. The treatment period begins with the administration of the first dose of study drug, 30 minutes prior to initiation of cyclophosphamide or doxorubicin (whichever occurs first), and continues until midnight on Study Day 3. A posttreatment final visit will occur after the end of the three day treatment period (Days 4-8). A total of 372 evaluable chemotherapy-naïve subjects will be enrolled in this multicenter trial. Eligible subjects will have a histologically proven cancer, be scheduled to receive a cyclophosphamide-based regimen of chemotherapy, and meet all other eligibility criteria. All subjects will receive cyclophosphamide ( $\geq 500\text{mg/m}^2$ ) and either doxorubicin ( $\geq 40\text{mg/m}^2$ ) or methotrexate ( $\geq 30\text{mg/m}^2$ ) administered over a period of less than 2 hours per agent. Thirty minutes prior to the administration of the chemotherapy regimen subjects will receive the first dose of study drug. Subjects will be randomized (1:1) to one of the following treatment arms for oral administration of study drug: 8 mg Ondansetron (BID x 3 days) + 15 mg Placebo Compazine Spansules (BID x 3 days) or 8 mg Placebo Ondansetron (BID x 3 days) + 15 mg Compazine Spansules (BID x 3 days). Efficacy data will be collected for each subject up until Study Day 3. The primary efficacy variable is the number of subjects with zero emetic episodes. Clinical adverse events will be recorded up until Study Day 3.

**Progress :** No subjects yet entered, patient screening is on-going.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 92/070	<b>Status:</b> Completed		
<b>Title:</b> Comparison of TLC D-99 Doxorubicin Liposome Injection versus Doxorubicin Injection in Metastatic Breast Cancer				
<b>Start Date:</b> 06/05/92	<b>Est. Completion Date:</b> Aug 95			
<b>Department:</b> Medicine, Hematology/Oncology Service	<b>Facility:</b> MAMC			
<b>Principal Investigator:</b> MAJ Robert B. Ellis, MC				
<table style="width: 100%; border: none;"> <tr> <td style="width: 50%; vertical-align: top;"> <b>Associate Investigators:</b>  LTC Howard Davidson, MC  LTC Luke M. Stapleton, MC  MAJ Patrick L. Gomez, MC  CPT Jennifer L. Cadiz, MC  CPT James S. D. Hu, MC </td> <td style="width: 50%; vertical-align: top;"> COL Joseph A. Paris, MC  MAJ Paul C. Sowray, MC  MAJ Kenneth A. Bertram, MC  MAJ Robert L. Sheffler, MC  MAJ Richard C. Tenglin, MC </td> </tr> </table>			<b>Associate Investigators:</b> LTC Howard Davidson, MC LTC Luke M. Stapleton, MC MAJ Patrick L. Gomez, MC CPT Jennifer L. Cadiz, MC CPT James S. D. Hu, MC	COL Joseph A. Paris, MC MAJ Paul C. Sowray, MC MAJ Kenneth A. Bertram, MC MAJ Robert L. Sheffler, MC MAJ Richard C. Tenglin, MC
<b>Associate Investigators:</b> LTC Howard Davidson, MC LTC Luke M. Stapleton, MC MAJ Patrick L. Gomez, MC CPT Jennifer L. Cadiz, MC CPT James S. D. Hu, MC	COL Joseph A. Paris, MC MAJ Paul C. Sowray, MC MAJ Kenneth A. Bertram, MC MAJ Robert L. Sheffler, MC MAJ Richard C. Tenglin, MC			
<b>Key Words:</b> cancer:breast, TLC D-99 doxorubicin liposome, doxorubicin				
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //		

**Study Objective:** To compare the cardiac safety of TLC D-99 (liposomal doxorubicin) with free doxorubicin using echocardiography, left ventricular ejection fraction measurements, and endomyocardial biopsies and to compare the efficacy of TLC D-99 with free doxorubicin HCL in the treatment of metastatic breast cancer.

**Technical Approach:** This will be a multicenter, randomized, parallel, open, comparative study in patients with metastatic breast cancer to compare the safety and efficacy of TLC D-99 and free doxorubicin HCl. Third party blinding will be implemented for evaluation of all radionuclide cardiac angiographies and cardiac biopsies. Growth Colony Stimulating Factor (G-CSF) therapy will be routinely given to both treatment groups in an effort to reduce the myelosuppression associated with doxorubicin administration. Therapy with either treatment will begin at 75 mg/m<sup>2</sup>. Dose escalation and reduction steps will be done based on patient tolerance of the drug. Separate randomization series will be used for patients with and without previous exposure to doxorubicin. Cardiac toxicity will be monitored by serial EKG's, echocardiograms, and resting and stress radionuclide cardiac angiography. To document pathologic changes seen with doxorubicin exposure, endomyocardial biopsies will be collected at a cumulative dose of 450 mg/m<sup>2</sup>. With any clinical or laboratory evidence of cardiac dysfunction or with progressive disease, treatment will be discontinued and the patient offered an alternate treatment program.

**Progress :** One subjected entered. Treatment was terminated do to cardiac toxicity.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/117		<b>Status:</b> Completed	
<b>Title:</b> A Randomized, Parallel Group, Double-Blind, Placebo-Controlled Phase II Study of Glycosylated Recombinant Human Interleukin-6 (Sigosix) in Patients Undergoing Combination Chemotherapy....breast cancer					
<b>Start Date:</b> 06/03/94			<b>Est. Completion Date:</b> Jul 95		
<b>Department:</b> Medicine, Hemotology/Oncology Service			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Robert B. Ellis, MC					
<b>Associate Investigators:</b>			MAJ Richard F. Williams, MC		
<b>Key Words:</b> cancer:breast, interleukin-6, Sigosix TM					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> //

**Study Objective:** 1) To evaluate the rate of hematopoietic recovery after myelosuppressive chemotherapy, and to determine any evidence of efficacy from r-hIL-6 which may be apparent in terms of attenuated thrombocytopenia or accelerated platelet count recovery. 2) To assess the safety and tolerance of administering repetitive daily subcutaneous doses of r-hIL-6 to patients with solid tumors after myelosuppressive chemotherapy. 3) To perform study-associated laboratory based investigations which will provide insight into the biologic actions of r-hIL-6 in vivo.

**Technical Approach:** Patients with advanced breast cancer who conform to the protocol eligibility criteria will be assigned to the study which consists of four treatment cycles of 21 days each. At the beginning of each cycle, all patients will receive CAF combination chemotherapy (Cyclophosphamide 3,000 mg/m<sup>2</sup> IV on day 1, doxorubicin (Adriamycin) 37.5 mg/m<sup>2</sup> IV on days 1 & 2; and Fluorouracil 600 mg/m<sup>2</sup> IV on day 1). All patients will receive G-CSF (Filgrastim, r-metHuG-CSF, 5 mcg/kg/day) daily SC days 3-14 and until the post nadir ANC count exceeds 10,000/mm<sup>3</sup>. They will also receive study drug (placebo or r-hIL-6, 10 mcg/kg/day SC) daily, starting on day 3 until the post nadir platelet count exceeds 10,000 platelets/mm<sup>3</sup> or for 23 days, whichever comes first. Patients will be prospectively randomized into two groups: Group 1 will receive placebo during cycles 1 & 2 and will receive r-hIL-6 during cycles 3 & 4; Group 2 will receive r-hIL-6 during cycles 1 & 2 and will receive placebo during cycles 3 & 4.

The primary parameter for analysis will be the percentage of patients who do not require platelet transfusions and the number of days each patient is dependent on platelet transfusions during cycles 1 or during cycle 2. A second primary efficacy variable will be the number of platelet transfusions required during cycle 1 or during cycle 2.

**Progress :** This study discontinued by the sponsor. No patients were screened or enrolled from MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/133	<b>Status:</b> On-going
<b>Title:</b> A Double-Blind, Randomized, Phase 3, Multicenter Study of Suramin and Hydrocortisone vs Hydrocortisone and Placebo in the Treatment of Patients with Metastatic, Hormone-Refractory Prostate Carcinoma		
<b>Start Date:</b> 05/19/95	<b>Est. Completion Date:</b> Jul 96	
<b>Department:</b> Medicine, Hematology/Oncology Service	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT James S. D. Hu, MC		
<b>Associate Investigators:</b>		
MAJ Kenneth A. Bertram, MC	LTC Robert D. Vallion, MC	
LTC Luke M. Stapleton, MC	MAJ Robert B. Ellis, MC	
MAJ J. Brantley Thrasher, MC	James H. Timmons, MD	
<b>Key Words:</b> Cancer:prostate, Suramin, Hydrocortisone		
<b>Accumulative</b> <b>MEDCASE Cost:</b>	<b>Est. Accumulative</b> <b>OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objectives:** To determine suramin's effect on pain, performance status, PSA, disease response, quality of life and survival in patients with hormone-refractory prostate carcinoma. Also to evaluate the safety of suramin.

**Technical Approach:** This study will be a double-blind, randomized, placebo-controlled, multi-center study of suramin plus hydrocortisone therapy versus placebo plus hydrocortisone therapy in 20 MAMC patients (total of 186 per treatment group) with prostatic carcinoma who have failed at least 1 course of prior hormonal manipulation. The primary outcome measurements will include changes in PSA level, disease response, quality of life, survival, time to progression, time to response and duration of responses. Patients will be stratified prospectively on the basis of PSA levels and presence of measurable disease and then randomly assigned to the suramin or placebo treatment groups. Patients will be given fixed doses of suramin or placebo, infused intravenously over a 1-hour period over a 78-day treatment period. Both arms will receive concomitant hydrocortisone. Primary efficacy determination will be determined on the basis of changes relative to baseline in pain score, analgesic use and performance status. Secondary efficacy measurements will be made on the basis of changes relative to baseline in other BPI scales, PSA changes, measurable disease response, and quality of life. Descriptive statistics will be provided for all demographic, efficacy and safety parameters. All tests will be 2-sided and conducted at the 5% level of significance. The level of significance will not be adjusted for the planned comparisons. Appropriate statistical methods will be applied to the various parameters and will include analysis of covariance, Cochran-Mantel-Haenszel analysis, and the Wilcoxon test.

**Progress :** One subject entered, recruitment continues.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/118	<b>Status:</b> On-going
<b>Title:</b> Phase II Study of Single Agent Thiotepa for Advanced, Hormone-Refractory Prostate Carcinoma		
<b>Start Date:</b> 06/03/94	<b>Est. Completion Date:</b> Dec 96	
<b>Department:</b> Medicine, Hematology/Oncology Service	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Timothy P. Rearden, MC		
<b>Associate Investigators:</b> MAJ J. Brantley Thrasher, MC MAJ Richard C. Tenglin, MC		Celestia S. Higano, MD MAJ Robert B. Ellis, MC
<b>Key Words:</b> cancer:prostate, thiotepa		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objective:** The purpose of this study is to evaluate the efficacy and toxicities of single agent thiotepa for advanced hormone-refractory prostate carcinoma.

**Technical Approach:** This is a non-randomized phase II study. All eligible patients with metastatic, hormone-refractory prostate cancer who are considered by their physicians to have a chance to benefit and also agree to participate will be entered. Patients will be initially staged with abdominal/pelvic C.T. scans, bone scans, chest radiographs, serum PSA, serum PAP, BUN, creatinine, liver function tests and complete blood count. All patients will receive thiotepa 50 mg/m<sup>2</sup> by intravenous administration at 28 - day intervals. Patients will be continued on therapy until: 1. disease progression is documented; 2. Unacceptable toxicities occur; or 3. the patient refuses further treatment for any reason. Any patient obtaining a complete response will receive two (2) additional courses of thiotepa past CR, and then be followed off therapy.

**Progress :** Two subjects entered in FY 95, one subject entered in FY 94.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/170	<b>Status:</b> On-going
<b>Title:</b> Phase 3 Trial of Gemcitabine Plus Cisplatin Versus Cisplatin Alone in Patients with Metastatic Non-Small Cell Lung Cancer		
<b>Start Date:</b> 07/21/95	<b>Est. Completion Date:</b> Sep 96	
<b>Department:</b> Medicine, Hematology/Oncology Service	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Luke M. Stapleton, MC		
<b>Associate Investigators:</b>		
CPT James S. D. Hu, MC	MAJ Kenneth A. Bertram, MC	
MAJ Robert B. Ellis, MC	LTC Robert D. Vallion, MC	
CPT John R. Caton, MC	MAJ Richard F. Williams, MC	
<b>Key Words:</b> cancer:non-small cell lung, gemcitabine, cisplatin		
<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	//

Study Objective: The primary objective of this study is to compare the survival of patients with Stage III and IV metastatic NSCLC treated with cisplatin alone to that of patients treated with the combination of cisplatin and gemcitabine.

Technical Approach: This is a randomized study of cisplatin monotherapy versus the combination of cisplatin and gemcitabine in patients with locally advanced (unresectable Stage IIIA or IIIB), or metastatic NSCLC who have received no prior chemotherapy regimens. Approximately 520 patients will be enrolled in this study and be randomized to receive either Regimen A or Regimen B. Regimen A is defined as follows: gemcitabine will be administered intravenously once each week for 3 weeks, followed by a 1-week rest period, and cisplatin will be administered intravenously once each cycle immediately after the first gemcitabine infusion of that cycle. This 4-week schedule defines a cycle of treatment. Multiple cycles will be administered. Regimen B is defined as follows: cisplatin will be administered intravenously once each cycle. Patients may receive a maximum of 6 cycles. It is anticipated that 10 to 15 patients will participate at Madigan.

Progress : New protocol just approved, no patients entered.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/055	<b>Status:</b> On-going
<b>Title:</b> Agrelin (Anagrelide) for Patients With Thrombocythemia		
<b>Start Date:</b> 02/04/94	<b>Est. Completion Date:</b> Jan 97	
<b>Department:</b> Medicine, Hematology/Oncology Service	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Luke M. Stapleton, MC		
<b>Associate Investigators:</b>		
MAJ Kenneth A. Bertram, MC	LTC Howard Davidson, MC	
MAJ Timothy P. Rearden, MC	MAJ Patrick L. Gomez, MC	
MAJ Robert B. Ellis, MC	MAJ Mark E. Robson, MC	
CPT James S. D. Hu, MC	MAJ Richard C. Tenglin, MC	
CPT Diana S. Willadsen, MC	LTC Robert D. Vallion, MC	
	MAJ Richard F. Williams, MC	
<b>Key Words:</b> thrombocythemia, Agrelin, safety, efficacy		
<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	01/20/95

**Study Objective:** To assess the safety and efficacy of Anagrelide in patients suffering from thrombocythemia of various etiologies.

**Technical Approach:** Patients who are 18 years or older, free of infection and have thrombocythemia due to a myeloproliferative disorder will be asked to participate. Those consenting will have a physical examination, complete blood count and serum chemistry and then be dispensed a three-month supply of drug. During treatment with Anagrelide, blood counts should be determined as often as needed to assure patient safety. Other test will be done as clinically indicated. Any patient whose thrombocythemia is unchanged ( $\pm 20\%$ ) after two weeks of treatment will be removed from the study. Those patients receiving benefit may remain on the study until the drug is released by the FDA or all trials are terminated. The data derived from the study will be analyzed by the sponsor.

**Progress :** 2 subjects have been entered. First subject is much improved since being on study. Second subject dose of hydrea needed to control resulted in too low wbc. She was started on study but never achieved a durable response. Patients was removed from study after several months of trial.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/187	<b>Status:</b> On-going
<b>Title:</b> A Study to Evaluate the Effect of Cisplatin/Epinephrine Injectable Gel (Product MPI 5010) When Administered Intratumorally for Achievement of Treatment of Goals in Accessible Tumors of Any Histology		
<b>Start Date:</b> 09/15/95	<b>Est. Completion Date:</b> Nov 96	
<b>Department:</b> Medicine, Hematology/Oncology Service	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Robert D. Vallion, MC		
<b>Associate Investigators:</b>		
CPT James S. D. Hu, MC	LTC Luke M. Stapleton, MC	
MAJ Robert B. Ellis, MC	MAJ Kenneth A. Bertram, MC	
MAJ Richard F. Williams, MC	CPT John R. Caton, MC	
R. Gauer	MAJ Robert L. Sheffler, MC	
<b>Key Words:</b> Tumors, Cisplatin, Epinephrine Injectable Gel		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objectives:** To evaluate the effect of MPI 5010 on local tumor volume and local tumor volume per patient. To assess achievement of an identified primary treatment goal selected for the most troublesome tumor following up to 6 weekly treatments of MPI 5010. To observe the time to response and the time to progression for the most troublesome tumor after treatment with MPI 5010. To assess improvement and stabilization in quality of life as measured by FACT-G/H&N. To evaluate the histopathology of injected lesions that respond to local treatment with MPI 5010.

**Technical Approach:** This will be a multi-center, open label study in approximately 60-65 evaluable patients with measurable and histopathologically confirmed accessible tumors of any histology except squamous cell carcinoma of the head and neck. Prior to the enrollment, the investigator must identify the patients's most troublesome tumor and one improvable primary treatment goal for that tumor. Patients with tumors measuring at least 0.5 cm<sup>3</sup> will be treated with 0.5 mL MPI 5010/cm<sup>3</sup> of tumor volume weekly for up to 6 treatments within 8 weeks or until patient objective complete response, which ever occurs first. Patients will return for an evaluation weekly for 4 weeks after the last treatment. Patients with a 100% reduction in volume of all treated tumors at the end of the Treatment Phase will be followed monthly for an additional 5 months or until time of tumor progression. Re-treatment of a tumor in follow-up in the case of disease or symptom progression may be performed if, in the opinion of the investigator, it will benefit the patient. Data analysis will include progress toward treatment goal, quality of life, tumor response, dosing, and safety. Appropriate statistical tools will be employed to measure and test each parameter in support of the objectives.

**Progress :** Protocol is awaiting final approval.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/105		<b>Status:</b> Completed	
<b>Title:</b> A Pilot Study of Granulocyte Colony-Stimulating Factor (G-CSF, Filgrastim) in the Empiric Treatment of Febrile Neutropenia Due to Myelosuppressive Chemotherapy					
<b>Start Date:</b> 05/07/93			<b>Est. Completion Date:</b> May 94		
<b>Department:</b> Medicine, Hematology/Oncology Service			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Diana S. Willadsen, MC					
<b>Associate Investigators:</b> CPT Steven E. Brilliant, MC MAJ Mark E. Robson, MC			CPT Diana S. Willadsen, MC CPT Curtis S. Hansen, RPH, MSC		
<b>Key Words:</b> neutropenia, GCSF, chemotherapy					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		//	

**Study Objective:** 1. To determine the median duration of neutropenia after admission for neutropenic fever in patients at Madigan Army Medical Center. 2. To determine whether a policy of delaying G-CSF therapy for 72 hours after admission with neutropenia and fever leads to prohibitively greater morbidity than a strategy of immediate administration of G-CSF.

**Technical Approach:** Patients with a non-myeloid malignancy who have received myelosuppressive chemotherapy and are admitted to Madigan Army Medical Center with a diagnosis of febrile neutropenia will be entered onto the study at the time of admission. Every attempt will be made to enroll consecutive patients with this diagnosis. Patients who received prophylactic G-CSF during the cycle in which they are admitted will be excluded, as will patients who are neutropenic before they receive chemotherapy. The first 10 patients (group I) will be observed to determine the duration of the nadir (absolute neutrophil count under 1000/mm<sup>3</sup>) after admission. The second 10 patients (group II) will receive G-CSF at a dose of 300 mcg/day by subcutaneous bolus if they fail to defervesce after 72 hours of broad spectrum empiric antibiotic therapy. Dose escalation will be instituted after 5 days of G-CSF therapy if criteria for discontinuation are not met. The last cohort of 10 patients (group III) will receive G-CSF within 12 hours of admission at the same dose as group II. The dose escalation scheme will be the same as for group II. Differences in mean and median nadir durations between the three groups will be evaluated by use of ANOVA analysis. Outcome of infection and in-hospital mortality will also be evaluated

**Progress :** Subject accrual is completed since departure of PI, however subject accrual continues at WRAMC. 2/3 of the planned subjects were entered.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/138	<b>Status:</b> On-going
<b>Title:</b> The Effect of Tamoxifen and Ionizing Radiation on Expression of Bcl-2, Bcl-x, and p53 in Breast Cancer Cells In Vitro		
<b>Start Date:</b> 06/16/95	<b>Est. Completion Date:</b> Mar 96	
<b>Department:</b> Medicine, Hematology/Oncology Service	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Richard F. Williams, MC		
<b>Associate Investigators:</b> MAJ Nyun C. Han, MC Katherine H. Moore, Ph.D.	MAJ Robert B. Ellis, MC MAJ Mark D. Brissette, MC	
<b>Key Words:</b> Cancer:breast, oncogenes, tamoxifen, radiation		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objectives:** The objective of this study is to define the molecular mechanism by which antitumor agents such as estrogen receptor antagonists and ionizing radiation initiate programmed cell death (apoptosis) in cultured breast cancer cells. Specific objectives are to examine the treated breast cancer culture cells for morphologic and biochemical evidence of apoptosis and to determine the time course for apoptotic death as well as that for changes in the level of bcl2 and p53 in the cells. Thereby, we will determine if changes in the level of these factors precede the onset of apoptotic death and provide evidence for the importance of modulation of the expression of these proteins as antitumor effects of these agents. Also, changes in other bcl2-related factors such as bax and bcl-x will be examined.

**Technical Approach:** Three breast cancer cell lines, MCF-7, MDA-MB-231, and ZR-75 cells, are currently available and express varying levels of estrogen receptor, bcl-2 and/or p53 molecules. Cells from each of these lines will be grown in the presence of estrogen for 24 hours, after which the medium will be treated with either tamoxifen or 4-hydroxytamoxifen, at 0.1 and 1.0 micromolar for six days. For the effects of radiation, cell will be grown in estrogen for 24 hours and then irradiated. At 24 hour intervals, cells from each experimental condition will be harvested and examine for apoptosis and for the level of expression of bcl2, bcl-x and p53. Morphologic and biochemical evidence for apoptosis in these cultures will be obtained by light microscopy and DNA agarose gel electrophoresis. Flow cytometry will be used to determine the fraction of apoptotic cells. Expression of the protein products of the three oncogenes will be determined by quantitative Western blot electrophoresis. The mean values and standard deviations for three separate cultures with each treatment at each time point will be determined. Statistical analysis will be performed using two way analysis of variance methods.

**Progress :** Quantitative western gel techniques have been established and optimized for BCL-2, BAX, and p53 in three human breast cancer cell lines (MCF-7, ZR-75, and MDA-MB 231). Western gel analysis of human BCL-X is currently being optimized. We have found that all three of these proteins are expressed in each of the three cell lines. We have demonstrated an inhibitory effect of tamoxifen at doses of  $10^{-6}$  M and  $5 \times 10^{-6}$  M after 6 days of incubation.



**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF MEDICINE, INFECTIOUS DISEASE  
SERVICE**

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/131		<b>Status:</b> On-going	
<b>Title:</b> A Double-Blind Multinational Trial Comparing Sorivudine [BV-araU] vs Acyclovir for the Treatment of Acute Localized Zoster and the Effect on Zoster-Associated Pain in Immunocompetent Subjects					
<b>Start Date:</b> 05/19/95			<b>Est. Completion Date:</b> Jul 97		
<b>Department:</b> Medicine, Infectious Disease Svc			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Ronald H. Cooper, MC					
<b>Associate Investigators:</b> COL Eugene T. Etzkorn, MC			CPT Thomas F. Burke, MC MAJ Joseph T. Morris III, MC		
<b>Key Words:</b> Zoster, Sorivudine, Acyclovir, immunocompetent					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> //

**Study Objectives:** To compare the safety and efficacy of sorivudine 40 mg once daily for 7 days vs. acyclovir 800 mg every four hours five times daily for 7 days in the treatment of acute localized zoster and the effects on zoster-associated pain and on healing of the skin lesions in immunocompetent subjects with trigeminal zoster or > 50 years of age.

**Technical Approach:** This is a randomized, double-blind comparative safety and efficacy trial of sorivudine vs. acyclovir in the treatment of acute localized zoster and the effect of zoster-associated pain and quality of life in immunocompetent subjects. It is anticipated that at least 348 subjects from approximately 35 centers will be enrolled into this trial. The subjects must have a localized rash consistent with zoster present for  $\leq$  72 hours; have trigeminal zoster or be >50 years of age; and have no evidence of an immunocompromising condition by medical history, physical examination or treatment history. Once stratified, the subjects will be randomized to either active sorivudine with acyclovir placebo or active acyclovir with sorivudine placebo. Subjects will be evaluated during and following treatment to determine their response to therapy. Clinical assessments will follow a rigid schedule with additional visits at the end of months 2 and 3 for those patients with continuing symptoms of post-herpetic neuralgia. Patients will be telephoned weekly to reinforce completion of diaries for assessments of efficacy, quality of life and pharmacoeconomic parameters. Clinical and laboratory adverse events will be assessed throughout the acute phase (Days 1-28) of the study. The two treatment groups will be compared with respect to the primary efficacy endpoint of total time (days) with severe or moderate pain associated with zoster during the six month study period using the Wilcoxon Rank-sum test.

**Progress :** 1 subject entered. Anticipate study will close in early November.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/132	<b>Status:</b> On-going
<b>Title:</b> An Open-Label, Multicenter Study of Clinafloxacin in the Treatment of Infective Endocarditis		
<b>Start Date:</b> 05/19/95	<b>Est. Completion Date:</b> Jul 97	
<b>Department:</b> Medicine, Infectious Disease Svc	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Ronald H. Cooper, MC		
<b>Associate Investigators:</b> COL Eugene T. Etzkorn, MC		
<b>Key Words:</b> Endocarditis, Clinafloxacin		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objectives:** To assess the efficacy of clinafloxacin in the treatment of patients with infective endocarditis.

**Technical Approach:** This study will evaluate the safety and efficacy of clinafloxacin in 50 patients (5 to 10 from MAMC) with infective endocarditis of bacterial etiology for survival rate, time to defervescence, time to sterile blood cultures and development of resistant pathogens. The dosage will be clinafloxacin 200 mg intravenously or by mouth every 12 hours for 4 to 6 weeks, up to 12 weeks maximum. The primary efficacy parameter is the microbiological eradication rate. Patients will be stratified on the basis of (1) right-sided vs left-sided endocarditis, (2) native valve versus prosthetic valve infection, and (3) pathogen recovered from blood cultured.

**Progress :** IRB approval just obtained, awaiting sponser go-ahead.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF MEDICINE, INTERNAL MEDICINE  
SERVICE**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/163		<b>Status:</b> Terminated	
<b>Title:</b> Utility of the Physical Examination to Assess Extracellular Volume Status					
<b>Start Date:</b> 09/03/93			<b>Est. Completion Date:</b> Jul 94		
<b>Department:</b> Medicine, Internal Medicine Svc			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Howard M. Cushner, MC					
<b>Associate Investigators:</b> MAJ Francis J. Landry, MC CPT Paul A. Lester, MC CPT Jeffrey R. Spina, MC			CPT Mary Jo K. Rohrer, MC MAJ Agnes K. Ohno, MC CPT Eric J. Ormseth, MC M.D. Gilman		
<b>Key Words:</b> physical examination,extracellular volume status					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$285.00		//	

**Study Objective:** To determine the sensitivity, specificity, and predictive value of clinical assessment in determination of extracellular volume status.

**Technical Approach:** A prospective study of 100 medicine ward patients ages 18-80. Patients will have one or more of the following: hyponatremia, elevated BUN of > 20, or elevated serum creatinine (absolute > 1.5). Physical exam will be performed prior to subjective history or chart review and before fluid resuscitation. Chart review will allow ordering of any pertinent test not found. Fluid resuscitation with NS, 2 liters over 24 hours, will be initiation. Post infusion labs will be drawn within 12 hours of infusion. The same investigator will repeat the post-infusion physical exam.

Blinded review of lab data, collected pre- and post-infusion, by two boarded nephrologist will serve as "gold standard" of volume status (volume depleted or not volume depleted). Five of seven predefined criteria must be met to be deemed "volume depleted". Subjects not responding within the 12 hour post volume repletion will be reviewed at 24-72 hours for further correction.

Analysis consists of 2 x 2 contingency tables with independent variable (physical exam criteria) and dependent variable (volume status).

**Progress :** Project terminated due to lack of time by PI. 14 subjects had been entered.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/066	<b>Status:</b> On-going
<b>Title:</b> Using Systems Methodology to Model and Deploy Ambulatory Care Resources		
<b>Start Date:</b> 03/04/94	<b>Est. Completion Date:</b>	
<b>Department:</b> Medicine, Internal Medicine Svc	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Duane J. Jeffers, MC		
<b>Associate Investigators:</b> W.P. Nichol Scott Iverson, MD	Tesfai Gabre-Kidan, MD Kenric W. Hammond, MD	
<b>Key Words:</b>		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** To: 1) Modify and validate two computer simulation models of ambulatory care resource allocation nearing completion at the Seattle VA Medical Center (SVAMC) ambulatory care clinic; and 2) adapt these "source" models for the ambulatory care clinics at the Madigan Army Medical Center (MAMC) and American Lake VA Medical Center (ALVAMC), as well as 3) perform sensitivity analysis and preliminary validation.

**Technical Approach:** Existing computer simulation models of the Ambulatory Care Service at SVAMC will be further refined and adapted to the MAMC and ALVAMC Ambulatory Care Services over a period of two and one-half years. The adaptation process includes surveying interested parties at the two sites, collecting the necessary data, and changing the "source" model. Sensitivity analysis, which assesses how the models respond to parameter changes, will be performed on all three models using the data to construct the models as well as data collected subsequently. Preliminary validation of the model with the aim of determining how well the model represents the system in question will also take place. Surveys will be conducted to investigate the impact of the model development process on organizational behavior. The models will be used, in a future project, to suggest intervention(s) to reconfigure one or more of the ambulatory care clinics, whereupon the intervention will be implemented and assessed.

**Progress :** This protocol is still in Phase I which involves developing a model of work processes and ambulatory care resources being used in the General Internal Medicine Clinic of the Seattle VA Medical Center. Established report of this work was submitted to the central office of the VA and a decision on further funding of this protocol is pending.

### Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 94/018

**Status:** On-going

**Title:** Impact of Adult Primary Care Clinic (APCC) on the Health Status of Patients and the Resource Utilization of MAMC

**Start Date:** 11/05/93

**Est. Completion Date:** Oct 95

**Department:** Medicine,  
Internal Medicine Svc

**Facility:** MAMC

**Principal Investigator:** MAJ Duane J. Jeffers, MC

**Associate Investigators:**

MAJ Sabrina A. Benjamin, MC

CPT Robert V. Gibbons, MC

LTC Jackie W. Saye, AN

COL Eric B. Schoomaker, MC

MAJ Francis J. Landry, MC

M. Lupo

Rhonda J. McColpin, DAC

**Key Words:** resource utilization, adult primary care clinic

**Accumulative**

**MEDCASE Cost:** \$0.00

**Est. Accumulative**

**OMA Cost:** \$1600.00

**Periodic Review:**

//

**Study Objective:** To determine the impact of a primary care clinic operating with managed care principles (the Adult Primary Care Clinic), on the health status of patients and overall resource utilization by enrolled clinic patients within a tertiary care medical center.

**Technical Approach:** Approximately 100 patients from a pool of 14,500 being enrolled into the Adult Primary Care Clinic will be selected by random number table to provide the sample. The study will measure two main outcomes: 1. The health status of patients and 2. Hospital Resource Utilization using predetermined yardsticks. A 12 month retrospective and prospective chart review will be used to determine resource utilization.

Comparison of before and after rates of compliance will be analyzed by Chi-square analysis for categorical variables. Analysis of Resource utilization will be done by paired T-test and multiple linear regression.

**Progress :** 400 subjects have been entered. Data collection is completed for the resource utilization of patients satisfaction portions of the protocol.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/083		<b>Status:</b> Completed	
<b>Title:</b> Converting Patients From One Anti-hypertensive to Another Drug[colon] Usage Study on Felodipine[colon] Cost Savings and Patient Outcomes					
<b>Start Date:</b> 04/01/94			<b>Est. Completion Date:</b> Sep 94		
<b>Department:</b> Medicine, Internal Medicine Svc			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Francis J. Landry, MC					
<b>Associate Investigators:</b> CPT James D. Horwhat, MC COL Richard J. Ferrell, MC			David Tomich, DAC Lisa Pinski, DAC		
<b>Key Words:</b> Anti-hypertensives:conversion, Felodipine, cost savings					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		//	

**Study Objective:** This study will determine outcomes of switching patients from more expensive calcium channel antagonists to a less expensive alternative. Such a change will 1) decrease antihypertensive therapy cost 2) cause no adverse effect on blood pressure control.

**Technical Approach:** Patients enrolled in the Adult Primary Care Clinic and referred by their physician will be eligible for entry if they are currently on either Nifedipine XL or Cardizem CD for hypertension. Physicians will be prompted to refer potential patients via an information sheet provided by the pharmacy after record review. Referred patients will be seen in the newly designated "hypertension clinic". The following information will be collected on initial referral: 1) Patient demographics to include age, race, major medical problems, previous HTN meds, and current hypertensive meds 2) Baseline in office blood pressure recording 3) Subjective symptom assessment profile (SSAP). Patients will be continued on current medication until 5 day self determination BPs are obtained. Patients or family members will be versed on the used of standardized and calibrated semiautomatic aneroid cuff (taken at 6-8 am, prior to medication and 6-8 pm). On return to clinic patients will be started on Felodipine 5 mg PO qd and titrated to achieve desired blood pressure control as determined by mean systolic and diastolic home BP evaluations and set by either 1) primary physicians goal BP for specific patients or 2) BP less than 140/90. Upon each visit to clinic (minimum 3--initial, one at one week then q 2 weeks and final visit at 1 month post optimal titration) results of 5 day self measured BP will be reviewed, repeat in office BP measurement recorded, review of side effects obtained, post questionnaires (SSA) completed. Descriptive statistics will be used to describe the number of patients achieving targeted BP at each level of dose titration, number and type of adverse side effects and number of patients discontinued from felodipine. Total cost of antihypertensive therapy, number of antihypertensives used and mean change in systolic and diastolic blood pressured will be compared pre and post medicine change using the student t-test.

**Progress :** 39 subjects completed the study. 85 % converted successfully to felodipine. 70% controlled on 5 mg. Blood pressures not adversely affected but improved. Subjective assessment revealed no significant change in symptoms at end of trial. Cost savings from conversion likely in excess of \$30,000 per year.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/048		<b>Status:</b> On-going	
<b>Title:</b> The Effect of Left Ventricular Hypertrophy on Diastolic Function at Rest and After Exercise					
<b>Start Date:</b> 12/16/94			<b>Est. Completion Date:</b> Sep 95		
<b>Department:</b> Medicine, Internal Medicine Svc			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Kenneth M. LeClerc, MC					
<b>Associate Investigators:</b> S.J. Fleet			MAJ Patrick A. Cambier, MC E.M. Osgard		
<b>Key Words:</b> Hypertrophy, diastolic function, exercise, rest					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		//	

**Study Objectives:** To evaluate dastolic function in two populations with left ventricular hypertrophy (LVT) at rest, after acute exercise testing, and following aerobic exercise training.

**Technical Approach:** A predetermined number (15-50 per group) of younger subjects (<45 years of age) with either isolated pathologic LVH (i.e. attributed to a primary medical problem) or physiologic LVH (attributable to exercise training) will undergo elective echocardiographic evaluation at rest and immediately after maximal exercise testing. Measures of diastolic function will be compared between these two groups. In addition, both groups will electively undergo a prescribed aerobic exercise program for 10 weeks and the effect on dastolic function will be re-assessed echocardiographically and differences within and between groups will be described. The echocardiographic studies will be analyzed by blinded observers for assessment of diastolic function using existing computerized analysis and compared using paired and unpaired T tests.

**Progress :** 11 subjects entered. Over 3000 echocardiograms records were screened. At this time, most of the subjects have nearly completed the intervention and have their post-intervention exercise test. Other subjects will be recruited through Dec 1995.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/179	<b>Status:</b> Completed
<b>Title:</b> Impact of Serial Neuroimaging Studies in Changing the TOAST Classification of Acute Stroke Patients		
<b>Start Date:</b> 09/02/94	<b>Est. Completion Date:</b>	
<b>Department:</b> Medicine, Internal Medicine Svc	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Stephen M. Salerno		
<b>Associate Investigators:</b> COL Eric B. Schoomaker, MC		MAJ Francis J. Landry, MC
<b>Key Words:</b> TOAST classification, acute stroke, neuroimaging		
<b>Accumulative</b> <b>MEDCASE Cost:</b>	<b>Est. Accumulative</b> <b>OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objective:** (1) Determine how often a second neuroimaging study is done in a patient with a new, but stable or improving neurologic deficit, (2) Determine whether more than one neuroimaging study in a stable patient with a new neurologic deficit has any impact on the patient's TOAST classification system or medical management.

**Technical Approach:** 200 inpatient charts with the discharge diagnosis of acute stroke and two neuroimaging studies will be examined retrospectively. The results of the initial neurologic exam, stroke risk factors, initial neuroimaging study and all ancillary studies to include carotid duplex, electro and echocardiograms, chest radiographs, and other blood and DSF tests will be recorded. These results along with the official radiology report of the initial neurologic imaging exam will be classified using the TOAST system.

The number of patients receiving a second neuroimaging study will be recorded. The indication for the study will be documented. In the cases where a second study was obtained for diagnostic purposes, the TOAST classification will be reviewed a second time and any changes recorded. The PI will perform the initial and final TOAST classification.

The amount of times the second neuroimaging study changed clinical management, defined as a change in medication or ordering of another diagnostic test documented in the physicians progress notes, will be recorded. Days of hospitalization of patients getting two or more neuroimaging studies will be compared to those who receive only one.

**Progress :** 206 subjects have been entered. In this study, for strokes of unknown etiology, multiple neuroimaging studies have potential to affect stroke classification and less often therapy. However, they have limited impact in the majority of strokes for which the etiology is more certain. Outcome is not significantly related to the quantity of neuroimaging studies obtained.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/037		<b>Status:</b> On-going	
<b>Title:</b> A New Method of Diagnosing and Treating Patients With Dyspepsia and Antibodies to <i>Helicobacter pylori</i>					
<b>Start Date:</b> 12/17/93			<b>Est. Completion Date:</b> Jan 95		
<b>Department:</b> Medicine, Internal Medicine Svc			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> G. H. Schwartz					
<b>Associate Investigators:</b>					
MAJ Amy M. Tsuchida, MC			MAJ Michael F. Lyons II, MC		
CPT Thomas P. Peller, MC			MAJ Kazunori Yamamoto, MC		
CPT Eric J. Ormseth, MC			LTC Gregory N. Bender, MC		
			MAJ Robert H. Sudduth, MC		
<b>Key Words:</b> dyspepsia, <i>Helicobacter pylori</i> , diagnosis, treatment					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		//	

**Study Objective:** To develop a cost effective algorithmic approach (ie. clinical pathway) that will predict which patients can be safely diagnosed and treated in a single outpatient visit for *Helicobacter pylori* induced symptoms of dyspepsia.

**Technical Approach:** Patients (300) with symptoms consistent with dyspepsia will be enrolled in the protocol. Patients will fill out a questionnaire designed to screen for those patients with symptoms consistent with dyspepsia. Those enrolled will all go through an esophageal-gastroduodenoscopy (EGD). Those patients with evidence of peptic ulcer disease will be so identified. Biopsies of gastric mucosa will be taken from all patients and sent to the lab for analysis of gastritis as well as for the presence of *H. pylori* using histologic methods. At endoscopy, biopsy material will also be tested for *H. pylori* using the CLO test. In addition, the ELISA and Flex Sure antibody tests for *H. pylori* will be performed. The patients will then be routed through radiology where they will receive an UGI barium study while at the same time a nasogastric tube (NGT) intubation of the esophagus and stomach and biopsies for *H. pylori* will be taken. Patients who do not have evidence of PUD, but with a positive diagnosis for *H. pylori*, will be randomized to four treatment arms each lasting two weeks. In the first, patients will be treated with the current standard at MAMC Gastroenterology Service, that being a two week course of amoxicillin and omeprazole. The second group of patients will be treated with a combination of metronidazole, peptobismal, and tetracycline plus omeprazole. Patients will be treated with omeprazole alone in the third arm, and in the fourth arm patients will be treated with a placebo. All patients will be treated for two weeks. Patients with evidence of PUD and with a positive diagnosis for *H. pylori* will be randomized to one of the first three treatment arms mentioned above. They will not be given a placebo. At the completion of the two week treatment all patients will then be given 28 days of ranitidine 150 mg twice daily, then 14 days of once daily treatment. Patients will then be followed at 2, 4, 8, 12, 20, 24, 28 and 32 weeks after treatment. A follow-up worksheet will be updated by the study coordinator. Follow-up serological blood test using the same *H. Pylori* antibody test will be performed. They will have a repeat EGD at 12 weeks after day #1 of treatment at which time they will have repeat biopsies for *H. pylori* and to assess ulcer healing if they originally had PUD. Data will be analyzed using Kappa test to determine sensitivities, specificities, and positive and negative predictive values.

**Progress :** 19 subjects have been entered. Our numbers continue to be low and we have stopped enrolling patients secondary to time constraints as we need to follow up these patients for one year after enrollment. Preliminary data has been very discouraging. Awaiting final word from sponsor in regard to terminating the project.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/111		<b>Status:</b> Completed	
<b>Title:</b> Prolonged Room Temperature Storage of DNA[colon] Comparison of a Standard Lysis Buffer With a Guanidinium Isothiocyanate Lysis Buffer					
<b>Start Date:</b> 04/21/95			<b>Est. Completion Date:</b> May 95		
<b>Department:</b> Medicine, Internal Medicine Svc			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> J.K. Waselenko, MC					
<b>Associate Investigators:</b> CPT Rodger K. Martin, MS			MAJ Robert M. Tuttle, MC		
<b>Key Words:</b> DNA:storage temperature					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//	

**Study Objective:** To determine the quantity and quality of DNA in a crude cell lysate of thyroid tissue stored guanidinium thiocyanate lysis buffer at room temperature for six weeks. To determine whether DNA stored for up to six weeks in a guanidinium thiocyanate lysis buffer at room temperature can serve as substrate for the polymerase chain reaction (PCR).

**Technical Approach:** Fresh frozen thyroid tissue will be homogenized in a glass grinder using either a solution containing guanidinium thiocyanate, beta-mercaptoethanol and sarcosyl (solution D) or a standard solution of Tris EDTA buffer in order to produce cell suspensions. Aliquots of this crude cell lysate will be used as the source for DNA for this study. DNA will be recovered at times 0, 3 days and weekly from weeks 1-6. Portions of the DNA will amplified with primers for thyroglobulin using PCR. This bench top study will provide some indication as to how quickly samples obtained from fine needle aspirations of the thyroid will need to be processed in order to allow optimal recovery of the nucleic acids. The study is largely descriptive. ANOVA will be used to compare quantities of DNA recovered at each time point (as determined by optical density at 260 nm wavelength) both over time within each group as well as between groups (standard Tris vs. Sol D).

**Progress :** 8 samples were studied. Study demonstarted that Solution D can be effectively used as a lysis/storage buffer for a dilute suspension of thyroid cells with subsequent nucleic acid recovery.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF MEDICINE, NEUROLOGY SERVICE**

### Detail Summary Sheet

**Date:** 30 Sep 95      **Protocol No.:** 93/080      **Status:** Terminated

**Title:** A Randomized Double-Blind, Cross-Over, Placebo-Controlled Clinical Trial of D-alpha-Tocopheryl Acetate (Vitamin E) as Add-On Therapy for Epilepsy in Adults

**Start Date:** 04/02/93

**Est. Completion Date:** Dec 94

**Department:** Medicine, Neurology Svc

**Facility:** MAMC

**Principal Investigator:** LTC William L. Clayton III, MC

**Associate Investigators:**

CPT Curtis S. Hansen, RPH, MSC  
N. Gore

Michele D. Leininger, RN  
D.J. Wilkie

**Key Words:**

**Accumulative**

**MEDCASE Cost:** \$0.00

**Est. Accumulative**

**OMA Cost:** \$0.00

**Periodic Review:**

//

**Study Objective:** To prospectively determine the effect of Vitamin E on seizure control in adults with frequent seizures.

**Technical Approach:** Volunteers of either sex who are over 18 years of age with a seizure disorder requiring treatment with antiepileptic drugs will be included in this study. Patients will be requested to keep a seizure calendar which will be reviewed monthly. After an observation period of 3 months, used to calculate seizure frequency, the pharmacy will issue either Vitamin E or placebo to be taken in addition to standard antiepileptic therapy. After 6 months the pharmacy will cross over the placebo/Vitamin E groups. At the end of 9 months the study will be discontinued. The patients will be informed of the results of the study at its completion. Any patient who benefited from Vitamin E will have the option of continuing therapy.

Statistical analysis will be by paired T-test for total number of seizures during the treatment period.

**Progress :** Terminated, no subjects entered. Did not get extramural funding.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/053		<b>Status:</b> On-going
<b>Title:</b> The Clinical Significance of Unilateral Rebound Nystagmus				
<b>Start Date:</b> 05/19/95		<b>Est. Completion Date:</b> Apr 95		
<b>Department:</b> Medicine, Neurology Svc		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Linda A. Marden, MC				
<b>Associate Investigators:</b>		MAJ Eugene F. May, MC		
<b>Key Words:</b> nystagmus:unilateral rebound, nystagmus:bilateral rebound				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//

**Study Objective:** To examine the clinical associations and localizing significance of unilateral rebound nystagmus.

**Technical Approach:** A review of 149 subjects with unilateral rebound nystagmus (URN) on neuroophthalmologic examination will be performed. These subjects will be divided into groups with URN from the right side or URN from the left side. Other abnormalities found on neuroophthalmologic examination will be analyzed for each group of patients. Additional clinical information will be obtained from records review, including imaging study results, presenting symptoms, known diagnoses, and will be analyzed for trends. This information will be analyzed descriptively to correlate localizing information and associated ocular motility findings.

**Progress :** Data has been collected on 153 subjects entered in the study. Statistical analysis needs to be completed. Unlike bilateral rebound nystagmus, which is highly correlated with cerebellar disease, the presence of URN is more likely a sign of brainstem pathology. The correlation of URN with H/sN, PPN, and GEN, all in the same direction, suggests a common etiology, most likely an asymmetry in the function of the brainstem vestibular system.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/153		<b>Status:</b> Completed
<b>Title:</b> Use of Proton Magnetic Resonance Spectroscopy (MRS) to Determine the Anatomic Location of a Pathologic Lesion in a Patient with Post-traumatic Movement Disorder				
<b>Start Date:</b> 09/21/94		<b>Est. Completion Date:</b> Oct 94		
<b>Department:</b> Medicine, Neurology Svc		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Jonathon Newmark, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> PET, focal dystonic ssyndrome				
<b>Accumulative MEDCASE Cost:</b> \$0.00		<b>Est. Accumulative OMA Cost:</b> \$0.00		<b>Periodic Review:</b> //

**Study Objective:** To use magnetic resonance spectroscopy (MRS) technology to verify and refine the anatomic localization of a lesion suspected on single proton emitted computed tomography (SPECT) in a unique patient.

**Technical Approach:** The patient will have 2 MRS sessions one week apart at the University of Washington Medical Center, Seattle. Each procedure will take approximately 60 minutes; no injections of dye will be used during either procedure. The patient will be required to go off anticholinergic medication during this one week period between the two examinations.

**Progress :** Approval of this protocol allowed us enough funds to study our patient at UWMC. For technical reasons our first attempt was not ideal, as the two recordings we made were done with coils which were not matched, and as a result the UW folks graciously allowed us to restudy the patient a few months later with no additional charge to the patient or to MAMC. The final version of the MR spec images were generated in late SEP 95 and are intriguing; they show signal voids in choline levels in basal ganglia ipsilateral to the patient's cerebral dysfunction, as well as decreased creatine levels in the off-anticholinergic state which correct when the patient takes drug. We believe that this may represent the first in vivo demonstration of localization of this sort of movement disorder in a patient with totally normal conventional MR images. We hope that, if accepted at the AAN and presented in San Francisco in March, we will get instructive comments from the movement disorders community which will allow us to refine the technique in such patients in the future; we do not plan right now to write further protocols until we can share these data with our colleagues.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/129		<b>Status:</b> On-going
<b>Title:</b> The Assessment of Motor Recovery After Stroke Induced Hemiplegia				
<b>Start Date:</b> 08/05/94		<b>Est. Completion Date:</b> Aug 94		
<b>Department:</b> Medicine, Neurology Svc		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Jonathon Newmark, MC				
<b>Associate Investigators:</b>		CPT Eric I. Hassid, MC		
<b>Key Words:</b> hemiplegia, stroke, motor recovery				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//

Study Objective: We hope to determine whether or not there exist certain consistent patterns of motor recovery after stroke. We also hope to be able to prognosticate about extent of motor recovery with relation to lesion site and size.

Technical Approach: Select patients from the neurology service who have sustained their first non-hemorrhagic stroke affecting motor function will obtain an MRI of the brain at about the 7 day post event mark for purposes of accurate neuroanatomical localization. These patients will be evaluated weekly to assess motor recovery. No additional studies which would not be part of good stroke care will be done. Clinical and statistical significance will be done by a statistician. The initial data analysis will be longitudinal, modeled upon that of Twitchell. Should trends develop of statistical significance, standard tests including ANOVA will be used as data points.

Progress : Twelve patients have been enrolled in this study. A change of staff halted work on this study for a few months. It is expected that patient accrual will now continue. At this point too disparate patients have been enrolled to conclude anything meaningful.

### Detail Summary Sheet

**Date:** 30 Sep 95      **Protocol No.:** 94/019      **Status:** On-going

**Title:** Use of CSF D-dimer Assay to Differentiate Subarachnoid Hemorrhage From Traumatic Lumbar Puncture

**Start Date:** 11/05/93

**Est. Completion Date:** Jun 94

**Department:** Medicine, Neurology Svc

**Facility:** MAMC

**Principal Investigator:** CPT David J. Wilke, MC

**Associate Investigators:**

LTC William L. Clayton III, MC

R.R. Larson

M.A. Elliott

D.C. Lipps

MAJ Mark D. Brissette, MC

CPT Dale T. Waldner, MC

**Key Words:** Assay:D-dimer, subarachnoid hemorrhage, lumbar puncture

**Accumulative**

**Est. Accumulative**

**Periodic Review:**

**MEDCASE Cost:** \$0.00

**OMA Cost:** \$100.00

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**Study Objective:** To prospectively determine the sensitivity and specificity of the CSF D-dimer assay in differentiating subarachnoid hemorrhage from traumatic lumbar puncture.

**Technical Approach:** This study will analyze cerebrospinal fluid (CSF) and plasma samples from 100 patients with a clinical history suggestive of subarachnoid hemorrhage (SAH). A lumbar puncture is done as part of the standard diagnostic workup. The fluid will be tested for D-dimer, xanthochromia and cell counts in addition to routine chemistries. A D-dimer will be obtained simultaneously from a peripheral blood sample that is routinely obtained for PT/PTT. The diagnosis of SAH will be determined by a combination of results from CT, LP, neuroimaging, and autopsy, which will serve as our "gold standard". Traumatic LP will be determined by the findings as noted above, plus the absence of SAH by standard diagnostic means.

**Progress :** 25 subjects have been entered. Data has not been compiled.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF MEDICINE, PULMONARY SERVICE**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/146		<b>Status:</b> On-going	
<b>Title:</b> Videoscopic Placement of Feeding Tubes[colon] Development of a Through the Tube Technique					
<b>Start Date:</b> 06/16/95			<b>Est. Completion Date:</b> May 98		
<b>Department:</b> Medicine, Pulmonary Svc			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Kurt W. A. Grathwohl, MC					
<b>Associate Investigators:</b> CPT James W. Thompson, MC LTC Bernard J. Roth, MC D.A. Dillard			CPT Robert V. Gibbons, MC J.D. Horwaht MAJ Patrick A. Cambier, MC		
<b>Key Words:</b> Feeding tubes: videoscopic placement, through-the-tube technique					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		//	

Study Objective: To describe a new technique for placement of small bowel feeding tubes.

Technical Approach: Ten ICU patients will be studied. An angiofiberscope (Olympus AF 22A) is placed through the center of a Corpak 10 F feeding tube which will be inserted under direct videoscopic guidance through the mouth or nose, into the esophagus and stomach. Thirty ml of viscous lidocaine or cetacaine spray will be used per standard procedure to provide local anesthesia of the mouth, pharynx and hypopharynx. The subject will be initially placed into Fowlers position and subsequently may be positioned into the lateral decubitus position. Air will be insufflated through the feeding tube into the stomach to allow visualization of the characteristic stomach anatomy. Using the deflectional capability of the angioscope, the tube/scope system will be advanced until the pylorus is identified. Once the pylorus is identified, the feeding tube will be advanced into the small bowel. Placement of the tube will be confirmed by the characteristic valvulae conniventes of the duodenum. A radiograph will be performed to confirm positive placement in the small bowel.

Progress : To date we have accomplished succesful placement of feeding tubes in all 8 subjects studied as well as in 8 patients, 7 of whom were intubated. 2 more subjects are planned for study.

### Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 94/023

**Status:** Completed

**Title:** The Effect of Using A Standard Mouthpiece vs Facemask on the Exercise Tolerance of Patients With Severe Chronic Obstructive Pulmonary Disease (COPD)

**Start Date:** 11/05/93

**Est. Completion Date:** Mar 94

**Department:** Medicine, Pulmonary Svc

**Facility:** MAMC

**Principal Investigator:** CPT James D. Horwhat, MC

**Associate Investigators:**  
CPT Jeffrey S. Strong, MC

LTC Bernard J. Roth, MC

**Key Words:** COPD, exercise, facemask

**Accumulative**

**Est. Accumulative**

**Periodic Review:**

**MEDCASE Cost:** \$0.00

**OMA Cost:** \$430.00

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**Study Objective:** To evaluate the possible effect of standard apparatus used to measure exercise parameters on the maximal exercise tolerance of patients with severe COPD. A secondary objective is to determine if pursed-lip breathing improves exercise capacity by decreasing oxygen demand or by improving ventilation-perfusion (VQ) relationships.

**Technical Approach:** We plan to perform 3 consecutive standard exercise tests on 15 patients with severe COPD. The three exercise trials will consist of one performed with a mouthpiece and noseclip, one with a facemask, and one without either. A one hour break will be provided between each trial, and the order of the trials will be randomly assigned for each individual. Multiple non-invasive parameters will be assessed. The data will be analyzed to evaluate for the presence of statistically and clinically significant differences in exercise tolerance between each technique of assessment.

**Progress :** 10 subjects entered. Manuscript in preparation.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/172		<b>Status:</b> On-going	
<b>Title:</b> The Value of Questionnaire Responses and Body Measurements in the Prediction of Obstructive Sleep Apnea in a Young Physically Fit Population					
<b>Start Date:</b> 09/15/95			<b>Est. Completion Date:</b> Jun 96		
<b>Department:</b> Medicine, Pulmonary Svc			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Joseph D. Kern, MC					
<b>Associate Investigators:</b>			V. Kapur		
<b>Key Words:</b> Sleep apnea, questionnaire. body measurements					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//	

**Study Objectives:** This study has two primary aims: to determine the prevalence of various symptoms and their specificity in obstructive sleep apnea syndrome (OSAS), and to examine the association of neck circumference, body mass index (BMI) and specific symptoms with sleep disordered breathing. Secondary aims are to determine if hypothyroidism needs to be excluded in individuals from this population being evaluated for OSAS, and to estimate period prevalence of OSAS in this population.

**Technical Approach:** Consecutive patients between the ages of 18 to 35 referred to MAMC for polysomnography will be eligible for inclusion in this cross sectional study. 200 eligible consenting participants will complete a symptom questionnaire and undergo a brief examination that includes neck circumference, blood pressure, weight and height measurements, and have serum thyroid stimulating hormone (TSH) evaluation prior to overnight polysomnography. An equal number of controls randomly sampled at routine health visits will complete the symptom questionnaire and have neck circumference, weight and height measurements performed. Questionnaire responses and anthropometric measurements will be compared between patients with OSAS and patients without OSAS and controls using the student's t test at  $\alpha=0.05$ . Sensitivity and specificity will be calculated for questionnaire responses. Questionnaire responses along with BMI, neck circumference (corrected for height), and hypertension will be evaluated using multiple linear regression techniques using apnea hypopnea index as the dependent variable. In addition, each of these factors will be evaluated individually by simple linear regression. The r and slope obtained for corrected neck circumference and BMI from linear regression will be compared with previously published estimates from other populations using the t test. The prevalence of hypothyroidism in all patients evaluated by polysomnography and just those with OSAS will be compared to the estimated prevalence in this age group (0) and the prevalence at a which screening for hypothyroidism is commonly recommended (2-5%) using the student's t test. A period prevalence will be calculated by dividing the number of cases detected in one year by the total referral population.

**Progress :** Protocol just approved and not yet started.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/162		<b>Status:</b> On-going	
<b>Title:</b> Exercise Capacity Following Radiation Therapy in Patients With Stages II and III Non-small Cell Lung Cancer					
<b>Start Date:</b> 09/03/93			<b>Est. Completion Date:</b> Jun 95		
<b>Department:</b> Medicine, Pulmonary Svc			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Timothy R. Murray, MC					
<b>Associate Investigators:</b> MAJ Rahul N. Dewan, MC			LTC Bernard J. Roth, MC MAJ Steven S. Wilson, MC		
<b>Key Words:</b> cancer:lung, radiation therapy, exercise capacity					
<b>Accumulative</b> <b>MEDCASE Cost:</b>		<b>Est. Accumulative</b> <b>OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$6390.00		//	

**Study Objective:** To study the physiologic effect of therapeutic radiation of the lung on exercise capacity in patients with stage II or III non-small cell lung cancer.

**Technical Approach:** All subjects will be evaluated within two weeks of initiation of radiation therapy (RT) and then 3, 6 and 12 months after initiation of RT. At each visit the subject will receive a brief history and physical exam and be asked to complete a questionnaire that will subjectively assess functional status. This data will be assessed and compared to objective data obtained from an exercise test conducted on a stationary, calibrated and electronically braked cycle. At exercise testing, subjects will be assessed at rest and at incremental work rates increasing at a fixed rate to between 20 and 50 watts per minute. Inhaled and exhaled gases will be measured. Vital signs will be documents every 20 seconds during exercise. Radiation treatment history will include total dose and calculation of lung volume irradiated.

Data will be examined for interval changes and correlated with radiation dose. A subset analysis will be attempted on patients receiving chemotherapy.

**Progress :** Fourteen patients have been enrolled in this study at MAMC. Nine patients with Stage III non-small cell lung cancer were studied 2 weeks prior to TLR and again 6 weeks after completion of TLC. These patients showed significant changes in certain exercise parameters occur early in the post TLR period. Although maximal work capacity was not significantly altered, the pattern of change suggests both a decrease in cardiac stroke volume and an increase in alveolar dead space.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/123		<b>Status:</b> Completed	
<b>Title:</b> Is the Use of Nose Clips Necessary in Adults Performing Routine Spirometry?					
<b>Start Date:</b> 03/17/95			<b>Est. Completion Date:</b> Jul 95		
<b>Department:</b> Medicine, Pulmonary Svc			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Joseph S. Pina, MC					
<b>Associate Investigators:</b> LTC Bernard J. Roth, MC			LTC Edward R. Carter, MC LTC William H. Cragun, MC		
<b>Key Words:</b> Spirometry, nose clips					
<b>Accumulative</b> <b>MEDCASE Cost:</b>		<b>Est. Accumulative</b> <b>OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		//	

**Study Objective:** The objective of this study is to determine whether the use of nose clips significantly affects spirometric values in adults performing routine spirometry.

**Technical Approach:** A randomized, blinded, prospective, crossover study is planned. Fifty normal patients (i.e., normal spirometry) and fifty patients with airflow obstruction (n=100) presenting to the Pulmonary function Laboratory for evaluation will be asked to participate. Additional subjects will be recruited from the Pulmonary Clinic and the Department of Medicine. Each patient will be asked to perform spirometry without nose clips and then again with nose clips. Half of each group will be randomized to perform spirometry without nose clips first and the other half will perform spirometry first with nose clips. The investigator involved with the pulmonary function testing will not know when the nose clips are being used. Each subject will perform a minimum of three acceptable spirometric maneuvers with and without nose clips. Standard pulmonary function values will be obtained, PEFR FEV<sub>1</sub>, FEF<sub>25-75</sub>, FVC and FEF<sub>75</sub>.

**Progress :** 91 subjects were entered. It was found that there were no statistical differences in each test with the obstructed, unobstructed, and combine groups in whether they used a nose clip or not. Manuscript has been written and submitted to the American Journal of Respiratory and Critical Care Medicine.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 93/104	<b>Status:</b> Terminated
<b>Title:</b> Does Sampling of the Lung With the Guidance of High Resolution CT Scan Improve the Utility of Bronchoalveolar Lavage or Transbronchial Biopsy		
<b>Start Date:</b> 05/07/93	<b>Est. Completion Date:</b> Jul 94	
<b>Department:</b> Medicine, Pulmonary Svc	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Joseph S. Pina, MC		
<b>Associate Investigators:</b>		
MAJ Cristopher A. Meyer, MC	MAJ Mary P. Horan, MC	
CPT Cynthia L. Clagett, MC	COL James L. Kelley, MS	
<b>Key Words:</b> lung, transbronchial biopsy, bronchoalveolar lavage, high resolution CT		
<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	//

**Study Objective:** To determine if high resolution CT (HRCT) scanning can be used to improve the yield of bronchoalveolar lavage (BAL) or transbronchial biopsy (TBB) in detecting and diagnosing interstitial lung disease.

**Technical Approach:** Consecutive patients with suspected interstitial lung disease referred to the pulmonary clinic will be considered for this study. The first twenty-five patients with ground glass opacification on HRCT scanning who pass certain exclusion criteria will be recruited. BAL and TBB will be performed in a segment of lung corresponding to an area of ground glass on HRCT scan and in an uninvolved segment as well. Therefore, "ground glass specimens" will comprise the cohort population and "uninvolved specimens" will act as the control population. Cell counts, cell concentrations and differential counts will be analyzed in each BAL specimen and pathology reviewed in each biopsy specimen. All cell concentrations will be scored to describe the intensity of the alveolitis present. Pathology will be scored based on whether the specimen is diagnostic or not. The cell counts, concentrations and scores from the ground glass BAL specimens will be compared to the uninvolved segment specimens. Pathology will be scored (normal, nondiagnostic, or diagnostic) and compared as well. If the BAL and TBB are nondiagnostic, an open lung biopsy will be recommended to the patient as the standard of care.

Routine chest X-rays, serum studies, skin testing and full pulmonary function testing will be performed on all patients as part of the routine evaluation of interstitial lung disease.

**Progress :** Study terminated after 4 patients entered. Diseases and patients could not meet inclusion criteria. Lack of time on the part of the PI was also noted.

### Detail Summary Sheet

**Date:** 30 Sep 95      **Protocol No.:** 94/178      **Status:** Terminated

**Title:** The Sensitivity and Specificity of High Resolution CT Scanning in the Detection of Alveolitis in Interstitial Lung Disease

**Start Date:** 09/02/94

**Est. Completion Date:** Mar 94

**Department:** Medicine, Pulmonary Svc

**Facility:** MAMC

**Principal Investigator:** CPT Joseph S. Pina, MC

**Associate Investigators:**  
MAJ Cristopher A. Meyer, MC

LTC Bernard J. Roth, MC

**Key Words:**

**Accumulative**

**Est. Accumulative**

**Periodic Review:**

**MEDCASE Cost:** \$0.00

**OMA Cost:** \$0.00

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**Study Objective:** To determine the sensitivity and specificity of the ground glass opacification on high resolution CT scanning of the chest in detecting alveolitis in the evaluation of interstitial lung disease

**Technical Approach:** Records of all high resolution CT scans of the chest over the past year will be reviewed in the Department of Radiology. The cases with no ground glass opacification seen on the scan will be checked to see if a bronchoscopy with bronchoalveolar lavage and transbronchial biopsy was done as part of the evaluation in the pulmonary clinic. If a diagnosis was obtained by transbronchial biopsy, open lung biopsy, or other modality, it will be noted. The subject's outpatient record, chest X-ray, etc., will also be reviewed to assess the stage and clinical extent of the disease process. The data obtained then will be analyzed to determine if any trends exist, such as diagnoses more likely to present with the lack of ground glass opacification.

**Progress : Progress :** Study terminated after 4 patients entered. Lack of time on the part of the PI was the reason.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 91/015	<b>Status:</b> On-going
<b>Title:</b> Controlled Trial of Positive Pressure Ventilation via Nasal Mask in Patients with Severe Chronic Air Flow Obstruction and Chronic Respiratory Failure		
<b>Start Date:</b> 12/07/90	<b>Est. Completion Date:</b>	
<b>Department:</b> Medicine, Pulmonary Svc	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Bernard J. Roth, MC		
<b>Associate Investigators:</b> MAJ Bruce S. Grover, MC		
<b>Associate Investigators:</b> LTC William H. Cragun, MC		
<b>Key Words:</b> positive pressure ventilation, air flow obstruction, nasal mask		
<b>Accumulative</b> <b>MEDCASE Cost:</b>	<b>Est. Accumulative</b> <b>OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$260.00	//

**Study Objective:** To determine if one eight hour period per week of ventilatory rest via nasal mask positive pressure ventilation will improve pulmonary function and exercise tolerance in patients with chronic air flow obstruction and chronic respiratory failure marked by an elevated arterial carbon dioxide.

**Technical Approach:** The study population will be both sexes, age >18 years, with severe COPD. The following baseline values will be obtained: age, weight, height, smoking status, medication list, chest x-ray, spirometry, formal lung volumes, MIP, MEP, DLCO, arterial blood gas measurement, pulse oximetry, end-tidal capnography, thyroid function tests, CBC, electrolytes, Karnofsky scale, dyspnea index, and 12 minutes walking distance. Spirometry, pulse oximetry, and end-tidal capnography will be repeated once weekly for four weeks. After four weeks, baseline studies will be repeated and an overnight polysomnography will be performed which includes electroencephalogram, electromyogram, electro-oculogram, airflow, chest wall and abdominal motion, pulse oximetry, and transcutaneous capnography. At this time the patient will be tested to determine if he tolerates intermittent positive pressure ventilation through a nose mask (nIPPV). Patients who tolerate nIPPV will be randomized to once weekly overnight nIPPV or nasal continuous positive airway pressure (nCPAP). Every 4 weeks during the 12 weeks of treatment, a repeat baseline evaluation will be done except that a transition dyspnea index rather than a baseline dyspnea index will be obtained. After 12 weeks of active therapy, the patients will be followed for an additional 12 weeks with 4 week evaluations as in the previous 12 weeks. Any change in pulmonary function, exercise tolerance, or dyspnea index will be compared between nCPAP and nIPPV patients using Student's T test. Significantly improved exercise tolerance, subjective dyspnea, Karnofsky scale, MVV, MIP, MEP, FVC, or PaCO<sub>2</sub> will be considered a positive result of nIPPV.

**Progress :** 5 subjects have been entered. Plan to do interim analysis to justify further data collection.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 92/024		<b>Status:</b> On-going	
<b>Title:</b> Resectable Bronchogenic Carcinoma[colon] Value of Routine Contrast - Enhanced Cranial MRI in Preoperative Staging					
<b>Start Date:</b> 01/03/92			<b>Est. Completion Date:</b>		
<b>Department:</b> Medicine, Pulmonary Svc			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Bernard J. Roth, MC					
<b>Associate Investigators:</b>					
MAJ Miquel J. Rovira, MC			MAJ Kevin L. Quinn, MC		
MAJ Frank A. Zimba, MC			MAJ Steven S. Wilson, MC		
<b>Key Words:</b> cancer, bronchogenic, MRI					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		//	

**Study Objective:** To determine the incidence of clinically occult brain metastasis in patients with resectable primary bronchogenic carcinoma.

**Technical Approach:** The subjects (100) for this protocol will be patients >18 years of age with primary bronchogenic carcinoma, Stage IIIa or less as determined by chest CT, who are neurologically intact. The patient will undergo a complete clinical neurological history and physical exam and enhanced cranial MRI to screen for brain metastasis. Patients with evidence of significant CNS pathology will be divided into four groups: (1) solitary lesion amenable to neurosurgical resection (2) significant brain pathology other than metastatic disease that would delay or preclude therapy (3) brain metastasis and (4) metastasis outside the brain. Patients in group 1 or 2 will undergo neurosurgical and/or radiation therapy evaluation for possible curative or palliative therapy. Patients in group 3 or 4 will undergo radiation therapy and/or hematology-oncology evaluation for possible palliative therapy. Patients in whom MRI revealed suspicious areas which are not definitely characteristic for metastasis will undergo brain biopsy using stereotactic localization. Patients refusing brain biopsy will be followed closely with periodic follow-up enhanced cranial MRI every three months. MRI and clinical data will be evaluated to determine the overall incidence of clinically occult brain metastases and the presence (if any) of any significant differences among primary cell types.

**Progress :** 5 subjects have been entered. WRAMC has been added as another site to improve accrual. Want 100 patients, have 30 so far.

## Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 90/099

**Status:** On-going

**Title:** Comparison of the Serum Effusion Albumin Gradient to Traditional Criteria for Transudates in Patients with Pleural Effusions Secondary to Congestive Heart Failure

**Start Date:** 08/17/90

**Est. Completion Date:**

**Department:** Medicine, Pulmonary Svc

**Facility:** MAMC

**Principal Investigator:** CPT Stephen M. Salerno

**Associate Investigators:**  
LTC Bernard J. Roth, MC

LTC William H. Cragun, MC

**Key Words:** pleural effusion, albumin, congestive heart failure

**Accumulative**

**Est. Accumulative**

**Periodic Review:**

**MEDCASE Cost:** \$0.00

**OMA Cost:** \$0.00

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**Study Objective:** To determine if the albumin gradient is a more effective criterion than Light's criteria to distinguish transudates from exudates in patients with congestive heart failure that have been treated with diuretics.

**Technical Approach:** Fifteen patients with clinically suspected congestive heart failure and chest radiograph evidence of pleural effusion will be studied. A thoracentesis to remove 50 cc of fluid will be performed and the following laboratory tests will be done on the fluid: albumin, total protein, glucose, LDH, bilirubin, cell count with cyto-spin differential, gram stain, and routine culture. A simultaneous sample of serum will be measured for albumin, total protein, LDH, bilirubin, and glucose. After three to five days of therapy for the congestive heart failure a repeat chest radiograph with bilateral decubitus view will be done. If pleural fluid persists, a repeat thoracentesis and laboratory tests will be done. If no fluid persists after three to five days, then the patient will be dropped from the study. Bilirubin ratio will also be assessed. The classification of the patients as exudate or transudate by serum effusion, bilirubin ratio, and Light's criteria will be compared between the two thoracentesis. McNemar's test for matched-pair data will be used to compare the albumin gradient results to Light's criteria.

**Progress :** 8 subjects have been entered. Despite a promising start, protocol has been difficult to complete because of stringent inclusion criteria, need for extra thoracentesis, and lack of manpower. We hope to complete the study in FY 96 with better education of physicians.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/139		<b>Status:</b> Completed	
<b>Title:</b> Total Lung Capacity Measured by a Medical Diagnostic Imaging Support System Planimetry Technique, Part II					
<b>Start Date:</b> 08/05/94			<b>Est. Completion Date:</b> Dec 94		
<b>Department:</b> Medicine, Pulmonary Svc			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Lisa L. Zacher, MC					
<b>Associate Investigators:</b> MAJ Donald V. Smith, MC CPT Daniel Walsh, MC			LTC William H. Cragun, MC P. Bryceland		
<b>Key Words:</b> Lung:capacity, MDIS, planimetry					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
<b>Periodic Review:</b>					//

**Study Objective:** To prospectively compare a planimetry method to calculate total lung capacity from a medical diagnostic imaging support (MDIS) system posteroanterior (PA) and lateral chest roentgenogram with total lung capacities derived from body plethysmography.

**Technical Approach:** This study will compare the planimetry technique outlined by Harris on a MDIS system posteror anterior and lateral chest roentgenograms with total lung capacities measured directly by body plethysmography in 100 patients being referred for pulmonary function testing that include measurement of lung volumes by body plethysmography. Each subject will undergo a chest roentgenogram and body plethysmography. Results from the two methods will be compared to obtain a correlation coefficient. In addition, regression equations will be obtained based on plethysmography values to determine if a new equation is necessary.

**Progress :** Sixteen males and eight females with obstructive (6), restrictive (6), and normal physiology (12) met study criteria. Good intraobserver and interobserver reliability was obtained with maximum differences of 3.2% and 5.1% respectively. A correlation coefficient of 0.91 was obtained for BPTLC versus PTLC. The simplicity, speed, reliability, economy, storage and transmission properties of the MDIS system's planimetry method are reasons to encourage its further clinical use.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/084		<b>Status:</b> Completed	
<b>Title:</b> Comparison of a High Resolution Computed Tomography Technique and Fiberoptic Bronchoscopy in the Evaluation of Hemoptysis					
<b>Start Date:</b> 04/02/93			<b>Est. Completion Date:</b> May 95		
<b>Department:</b> Medicine, Pulmonary Svc			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Lisa L. Zacher, MC					
<b>Associate Investigators:</b> MAJ James D. Pike, MC			CPT Lynn M. Keenan, MC MAJ Cristopher A. Meyer, MC		
<b>Key Words:</b> hemoptysis:CT, fiberoptic bronchoscopy					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$100.00
					<b>Periodic Review:</b> //

**Study Objective:** To prospectively compare the contributions of high resolution computed tomography technique (HRCT) and fiberoptic bronchoscopy (FOB) in evaluation of patients presenting with hemoptysis.

**Technical Approach:** Study patients would receive a standardized initial work-up to include history and physical examination, screening labs and a PA and lateral chest X-ray. Demographic data to include age, sex, tobacco history, and frequency and amount of hemoptysis will be noted on the data sheet. Chest X-rays will be designated as normal, abnormal, but non-localizing, or abnormal and localizing. Where there is a discrepancy between the radiologist and the bronchoscopist, the more abnormal interpretation will be utilized.

The radiologist will need to have experience reading HRCT. If such a qualified person cannot be found at other participating institutes, CT scans will be forwarded to MAMC Radiology for interpretation. If more than one radiologist is involved in reading the HRCT examinations, five films will be exchanged to check for interobserver variability. The radiologist will also have access to chest x-rays but be blinded to FOB results and given only the history of hemoptysis. The bronchoscopist ideally will be blinded to CT results but in particular cases where CT scans are available to the bronchoscopist they can be utilized to direct sampling techniques as long as FOB visual findings are properly recorded. If contract CT has already been done and demonstrates source of bleed, additional HRCT views would not be obtained. The order of obtaining HRCT and FOB in all patients need not be uniform. Data will be analyzed looking at clinical characteristics and roentgenographic findings associated with certain diagnosis. HRCT-FOB correlations will focus on the individual and combined efficacy in predicting and/or diagnosing the etiology of hemoptysis.

Statistical significance of observed differences between the two groups (FOB and HRCT) will be by Chi-Square. Multivariate analysis will be made by the stepwise linear discriminate analysis method to determine risk factors associated with lung cancer.

**Progress :** 40 patients were entered. The etiology of hemoptysis was attributed to the following diagnosis: bronchitis (33%), bronchiectasis (23%), bronchitis/bronchiectasis (5%), unknown (25%), tracheal tumor (3%), and miscellaneous (13%). High resolution CT was diagnostic in fourteen; FOB was diagnostic in an addition seven patients. The two modalities combined proveded a 68% diagnostic factor.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF NURSING**



### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/154		<b>Status:</b> On-going	
<b>Title:</b> A Descriptive Study of the Development of Critical Pathways in the Perioperative Nursing Department in Two Pacific Northwest Hospitals					
<b>Start Date:</b> 08/18/95			<b>Est. Completion Date:</b> Sep 95		
<b>Department:</b> Nursing			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> B.J. Ascelrod					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Critical pathways: perioperative nursing					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//	

**Study Objective:** This study is concerned with discovering what steps are used by perioperative nursing departments in the development of critical pathways. In addition, the study is concerned with the relationship, if any, between the actual steps used and written literature on the subject. Further, a final concern is what influence did any standard have on the development of critical pathways (example AORN standards)

**Technical Approach:** This study is a description of the development of critical pathways in the perioperative nursing department in two Pacific Northwest hospitals. The purposes of the study were to describe the development of critical pathways in the perioperative nursing department of an acute care hospital and to compare the development of critical pathways to the current literature on the subject. Data collected were examined from the perspective provided by an integrated model based on systems theory and the New England Medical Center Hospital's "Nursing Case Management Model".

The study used a purposive convenience sample of two perioperative nursing departments. Participants were the individuals designated as coordinators for the development of critical pathways within the departments. Data were collected through face-to-face interview and analysis of documents within a comparative case study design. The actual development of critical pathways was compared to principles and prescriptions for developing critical paths as reported in the literature.

**Progress :** Study had just been approved so no progress as of yet.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/078		<b>Status:</b> Terminated	
<b>Title:</b> Impact of ETS with ZEEP vs. PEEP on Physiology of Premies					
<b>Start Date:</b> 02/17/95			<b>Est. Completion Date:</b> Sep 96		
<b>Department:</b> Nursing			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Pamela S. Birgenheier, AN					
<b>Associate Investigators:</b> Lori A. Loan, MSN, RNC			LTC Joanna C. Beachy, MC Suzanne K. Wilson, MSN, RN		
<b>Key Words:</b> Suctioning:endotracheal, Pressure: positive end-expiratory, Pressure:zero end-espiratory pressure					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
<b>Periodic Review:</b>					//

**Study Objective:** 1. Is there a difference in oxygenation (SaO<sub>2</sub>), intracranial pressure (ICP), heart rate (HR), transcutaneous carbon dioxide tension (tcCO<sub>2</sub>), mean airway pressure (Paw) and blood pressure (MAP) when premature infants receive endotracheal suctioning (ETS) using positive end-expiratory pressure (PEEP) versus zero end-expiratory pressure (ZEEP)? 2. Is there a difference in the amount of secretions recovered after 3 ETS procedures with PEEP versus 3 ETS procedures with ZEEP in premature infants?

**Technical Approach:** Using a multisite study (2 military medical centers and one civilian medical center) we propose to compare the two types of ETS procedures /ETS PEEP:ETS ZEEP for their effect on the physiology of 60 premature infants (20 per site). Each infant will serve as their own control for 6 ETS procedures (3 ETS PEEP; 3 ETS ZEEP) administered in sets of three with random assignment to initial group and balanced randomization at each medical center. Data will be collected continuously (10 samples per second) and simultaneously for the following dependent variables: SaO<sub>2</sub>, ICP, TcCO<sub>2</sub>, HR, Paw, MAP, RR for the period starting 5 minutes prior to ETS and continuing until 10 minutes post ETS for each of six ETS procedures. The efficacy of each method will be measured using recovered secretions measured on a Mettler balance. Data will be analyzed using repeated measures ANOVA for within group and between group changes. Appropriate post-hoc analysis will take place.

**Progress :** This protocol was terminated due to lack of funding.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/116		<b>Status:</b> Completed	
<b>Title:</b> Effects of Military Parents' Separation on Children					
<b>Start Date:</b> 06/09/93			<b>Est. Completion Date:</b> Oct 93		
<b>Department:</b> Nursing			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Pamela S. Birgenheier, AN					
<b>Associate Investigators:</b>			P.A. Maniaci		
<b>Key Words:</b> parent,child separation, military parents					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//	

**Study Objective:** (1) When separated from a parent for military duty, do school-aged children from military families have more behavior problems than military children not separated from a parent? (2) Do school-aged children separated from their mothers for military duty demonstrate different behaviors than those children separated from their fathers for military duty?

**Technical Approach:** This is a descriptive study using a questionnaire. A minimum of 360 subjects, children of active duty military, ages 6 - 14 of both sexes will be used. Three main groups will be used consisting of 120 subjects each. These groups will be determined by (1) Father absent, (2) Mother absent, and (3) No Parent absent. Questionnaires will be provided to parents wishing to participate and meeting the entry criteria. They will be instructed to have the child's primary care giver furnish the information required by the questionnaire.

For data analysis the children will be matched as closely as possible across three areas of performance (social, activities, and school) for age, sex and parent rank. An ANOVA will be performed for statistical analysis to compare the children in the three groups in the three different areas of performance.

**Progress :** 150 subjects were enrolled, 127 met the study criteria. Scoring and analysis of Child Behavior Checklist has been completed. Review of the data showed only 6 children had noted behavioral problems, 4 of these children were separated from a parent. With scoring and statistical data completed, no statistical data was found to support the hypothesis that children separated from a parent for military duty have more behavior problems than children not separated from a parent.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/175		<b>Status:</b> Completed	
<b>Title:</b> Planning for Pregnancy[colon] The Experience of Women With Diabetes					
<b>Start Date:</b> 09/02/94			<b>Est. Completion Date:</b>		
<b>Department:</b> Nursing			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Gwendolyn M. Brown, RN, BSN					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> pregnancy, diabetes					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//	

**Study Objective:** (1) To determine the percent of women who have knowledge and understanding about the relationship between poor glycemic control and birth defects prior to becoming pregnant, (2) To assess the frequency and quality of pregnancy planning information women with diabetes receive from providers, (3) To determine the percent of women with diabetes who plan their pregnancies and who optimize their glycemic control prior to pregnancy, (4) To identify barriers and motivators associated with pregnancy planning and preconception glycemic control, across a broad socioeconomic population base, (5) To determine the rate of birth defects associated with diabetes and pregnancy in Washington State.

**Technical Approach:** Patients enrolled will be mailed a set of questionnaires designed to assess a variety of factors related to their experiences with diabetes. The study also involves home interviews by a member of the study interview team. This informal interview will last about 1 to 1 1/2 hours. Brief notes will be taken and if agreed to, the interview will be tape recorded to that the information given can be recorded accurately. Patients will also be asked to sign a release of information form to obtain selected information from their hospital records: blood sugar and glycosylated hemoglobin values, complications during pregnancy, and newborn assessment of their babies.

**Progress :** 8 subjects were enrolled. Patient accrual is complete. Data analysis is in progress.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/114		<b>Status:</b> Completed	
<b>Title:</b> The Effects of Exercise on Pregnancy					
<b>Start Date:</b> 06/16/95			<b>Est. Completion Date:</b> Apr 95		
<b>Department:</b> Nursing			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> A. Buchanan					
<b>Associate Investigators:</b>			Lori A. Loan, MSN, RNC		
<b>Key Words:</b> Pregnancy, exercise					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		//	

**Study Objective:** The purpose of this study is to examine the differences between women who have regularly participated in exercise during the second and third trimesters of pregnancy and those who do not.

**Technical Approach:** This study will examine the files of 80-200 women involved in the Pregnant Soldier Wellness Program (PSWP) for data which will provide the desired information. The specific areas that will be examined are exercise habits, gestation age, fetal birth weight, APGAR scores (infant assessment) and complications experienced. The data will be analyzed using the ANOVA statistical program to determine if exercise during pregnancy does effect outcome.

**Progress :** 82 subjects were enrolled in FY 95. The results of the surveys of these 82 subjects indicated that the quantity of exercise a woman participates in during pregnancy has little effect on the size or condition of the child at birth. Results showed exercise was only significant in the Apgar score one minute after birth.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/110		<b>Status:</b> Completed	
<b>Title:</b> Psychology of Pregnancy[colon] Peace and War-time					
<b>Start Date:</b> 05/06/94			<b>Est. Completion Date:</b> Sep 94		
<b>Department:</b> Nursing			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Susan L. Burroughs, AN					
<b>Associate Investigators:</b>			LTC Irene M. Rich, AN		
<b>Key Words:</b> pregnancy, peace,war-time psychology					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//	

**Study Objective:** To explore peace and war-time differences in the psychological experience of pregnancy.

**Technical Approach:** Three questionnaires will be used in the research. 1) A newly developed pregnancy questionnaire, the R-PAAS, will be used to look at feelings that women have about the experience of pregnancy, and how these feelings vary over a one week period. 2) A questionnaire called the SCL-90-R will be used to look at symptoms women have experienced over the past week. 3) Background information about occupation, education, and medical history will be obtained using a demographic information sheet.

**Progress :** Data analysis is completed, however no abstract was available at this time.

### Detail Summary Sheet

**Date:** 30 Sep 95      **Protocol No.:** 95/116      **Status:** Completed

**Title:** The Association of Menstrual Cycle Phases with Clinically Significant Nausea and Vomiting Following Laparoscopic Surgery

**Start Date:** 04/21/95

**Est. Completion Date:** Aug 95

**Department:** Nursing

**Facility:** MAMC

**Principal Investigator:** CPT Robert J. Bush, MC

**Associate Investigators:**

CPT Jacqueline A. Stark, MC

CPT Derek M. Williams, MC

CPT Wesley N. Hudson, MC

CPT Thomas Simpkins, MC

**Key Words:**

**Accumulative**

**MEDCASE Cost:** \$0.00

**Est. Accumulative**

**OMA Cost:** \$0.00

**Periodic Review:**

//

**Study Objective:** The purpose of this study is to describe the relationship between the phases of the menstrual cycle and clinically significant post-operative nausea and vomiting following gynecologic laparoscopic surgery.

**Technical Approach:** This study will draw from a population of females between the ages of eighteen and forty-five years of age who are undergoing gynecological laparoscopic procedures at MAMC. The intended sample of 90 (n=90) will be drawn from those patients who enter through the Same Day Surgery Center. The researchers will collect a ten milliliter blood sample during an IV start that will later be analyzed for progesterone levels. This hormone level will then allow for accurate reporting of the subject's menstrual cycle phase. A standard, safe and appropriate anesthetic will then be provided. During the PACU stay, the subject will be monitored for the occurrence of clinically significant nausea and vomiting. The nausea/vomiting data will then be correlated with the menstrual phase data and analyzed using a Chi-square method for statistical significance.

**Progress :** 38 subjects were entered. Analysis of the data resulted in no statistically significant relationship between phase of the menstrual cycle and the incidence of clinically significant nausea.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/118		<b>Status:</b> Completed	
<b>Title:</b> Crisis Intervention With Critical Care Families					
<b>Start Date:</b> 06/09/93			<b>Est. Completion Date:</b> May 94		
<b>Department:</b> Nursing			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mary Ann Carr, AN					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> critical care, family intervention					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//	

**Study Objective:** To measure the effect of a family crisis intervention program on family need satisfaction, family functioning, and patient stress following acute myocardial infarction (AMI).

**Technical Approach:** Two groups of 50 patients will be involved in this study. The design is a post-test-only control group design with random assignment of subjects. The experimental group will receive family crisis intervention on a minimum of three occasions during the hospitalization. A family representative will complete the Family Need Satisfaction/Family need Importance and the Family Adjustment of Medical Stressor Questionnaires; patients will complete the Stress of Discharge Assessment Tool (SDAT) within 48 hours of discharge. Multivariate statistics will be done to measure for significant outcomes differences between groups as a result of the independent variable: crisis intervention. Results will also provide military nurses with a theoretical crisis intervention process model to use with all patients and families in similar life-threatening medical and separation crisis.

**Progress :** 59 patient/family member pairs entered. Statistical analysis revealed no significant difference between blind-control and experimental groups.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/009	<b>Status:</b> Completed
<b>Title:</b> Identifying Process Variation via Risk-Adjusted Outcome		
<b>Start Date:</b> 11/18/94	<b>Est. Completion Date:</b> Jun 95	
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> K.J. Dolter		
<b>Associate Investigators:</b> S.B. Henry		Diane M. Pierson, BS, BA, CCRN
<b>Key Words:</b> Quality of Care:cardiopulmonary bypass, mortality rates		
<b>Accumulative</b> <b>MEDCASE Cost:</b>	<b>Est. Accumulative</b> <b>OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objective:** This is a descriptive study to determine 1) the differences between DOD medical center actual and predicted CABG mortality rates, 2) the hemodynamic knowledge and hemodynamic measurement and treatment practice of nurses and physicians caring for patients in DOD medical centers, 3) the relationship between hemodynamic knowledge and hemodynamic measurement and treatment practice of nurses and physicians caring for CABG patients in DOD medical centers, 4) the differences between nurse hemodynamic knowledge and hemodynamic measurement and treatment processes at DOD medical center with higher than expected mortality rates and DOD medical centers with lower than expected mortality rates, and 5) other unit and provider characteristics and processes of DOD medical centers with higher than expected CABG mortality rates and DOD medical centers with lower than expected CABG mortality rates.

**Technical Approach:** Phase I will be the identification of medical centers which perform CABGS and a collection of DOD discharge abstract data. Phase II-A will identify 6 of the 13 medical centers at which on-site visits will be performed; questionnaires on observation, knowledge tests, organizational questionnaire and computer simulation will be given to nurse/physician care providers designated. Phase II-B will identify 7 of the 13 medical centers not undergoing on-site visits; nurse/physician care providers will be given knowledge tests and organizational questionnaires. Phase II-C will be an audit of patient charts from the first 6 months of 1994 and during the 2 week site visit at each DOD medical center undergoing on-site visit, approximately 300 charts.

**Progress :** A risk-adjusted model of CABGS mortality was developed using 6 DOD medical centers. This showed the following significant factors: acute myocardial infarction, age, repeat CABGS, female sex, diabetes mellitus, and hypertension. All DOD medical centers had actual mortality that was less than that predicted by the risk-adjustment.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/034		<b>Status:</b> Completed	
<b>Title:</b> The Role of the Critical Care Nurse in Resolving Ethical Conflicts Resulting From Disagreement Regarding Treatment Between the Patient or Intimate Others and the Health Care Team[colon] A Qualitative Study					
<b>Start Date:</b> 11/18/94			<b>Est. Completion Date:</b> Jan 95		
<b>Department:</b> Nursing			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Joan T. W. Lancaster, AN					
<b>Associate Investigators:</b>			T. Simpson		
<b>Key Words:</b> patient treatment:patient disagreement, critical care nurse					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//	

**Study Objectives:** The purpose of this study is to examine and explore the role of the critical care nurse in resolving ethical conflicts that result from disagreement regarding treatment between the patient or the intimate others and the health care team.

**Technical Approach:** A convenience sample of registered nurses from the Medical Intensive Care Unit will be studied to explore the role of the nurse within ethical conflicts involving others and the health care team. The study will be conducted using 30-45 minute in-depth interviews and a demographic questionnaire. The interviews will be conducted individually using a semi-structured interview. The interview will begin with a brief introduction to explain the purpose of the interview to the subject, and continue with open-ended questions designed to elicit a description of 1) a patient care situation involving disagreement regarding treatment between the patient or intimate others and the health care team, and resulting in ethical conflict; 2) the type of ethical conflict caused by the described patient care situation; 3) how the nurse participated in the resolution of the ethical conflict; 4) the final outcome of the patient situation, and 5) how, in retrospect, the nurse would change their participation in the resolution of the ethical conflict. Prior to the interview the nurse will complete a demographic data questionnaire which will be used to construct a profile of the nurses who participated in the study. Using content analysis and descriptive statistics the data collected from the tape-recorded and transcribed interview will be analyzed to develop recurring themes and categories related to the specific aims of the study.

**Progress :** Study showed that treatment disagreements between patients or families and the health care team surrounded the issues of resuscitation, aggressive versus nonaggressive treatment, and withdrawal versus continuation of life supportive therapy. These disagreements resulted in a wide variety of ethical conflicts.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/117		<b>Status:</b> On-going	
<b>Title:</b> Exogenous Surfactant Therapy in Premature Infants					
<b>Start Date:</b> 06/09/93			<b>Est. Completion Date:</b> Sep 94		
<b>Department:</b> Nursing			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Deborah J. Leander, AN					
<b>Associate Investigators:</b> LTC Barbara S. Turner, AN			LTC Joanna C. Beachy, MC CPT William D. Glover, AN		
<b>Key Words:</b> surfactant, premature infants					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		//	

**Study Objective:** To examine two types of surfactant (Exosurf & Survanta), 3 methods of administration, and the resulting neonatal physiologic responses and outcomes. A secondary aim will be to determine the relationships between type of surfactant and administration technique, nursing assessed neonatal clinical cues of a hemodynamically significant patent ductus arteriosus, and neonatal outcomes.

**Technical Approach:** This is a prospective, quasi-experimental study, in which selected physiologic parameters will be monitored during exogenous surfactant administration in a convenience sample of 24 premature infants. Subjects will be randomly divided into one of three administration groups. A control group receiving no surfactant would not be appropriate as it would mean the infants would receive less than the standard of care.

The convenience sample will consist of 24 neonates, with the diagnosis of RDS, who will receive exogenous surfactant using rescue therapy. The three groups will be: 1) n=12, Exosurf administered by sideport adapter. 2) n=6, Survanta administered by feeding tube through endotracheal tube. 3) n=6, Survanta administered through double lumen ET tube. After consent is obtained and electronic monitors applied, baseline data will be collected for 10 minutes after which either Survanta or Exosurf will be administered by the predetermined route. The infant will be ventilated during the procedure using NICU SOPs. At completion of the surfactant administration, data collection will continue for 2 hours. Nurses will be free to make whatever adjustments they deem necessary in response to the lung compliance changes using their own judgment or in consultation with the physician.

Descriptive statistics obtained from the data will be categorized into critical ranges for each of the data collection periods. Demographic data will be coded and analyzed.

**Progress :** 52 subjects were entered. Group data analysis continues.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/175	<b>Status:</b> On-going
<b>Title:</b> A Comparison of Skin Microbes Under Two Types of Temperature Probe Covers Used on Premature Newborns		
<b>Start Date:</b> 08/18/95	<b>Est. Completion Date:</b> Sep 96	
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> Lori A. Loan, MSN, RNC		
<b>Associate Investigators:</b> Debra DePaul, RN CPT Wade K. Aldous, MS		
K.K. Marbut MAJ Pamela S. Birgenheier, AN		
<b>Key Words:</b> Microbes, probe covers, NICU		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objectives:** This is a descriptive pilot study to determine if the temperature probe covers in current use in the NICU contribute to nosocomial infections by providing an environment for normal skin microbes to colonies.

**Technical Approach:** Two types of probe covers are currently used in the MAMC NICU. One type has a reflective exterior surface and a type of foam tape adhesive on the interior surface (Probe Cover A). The second type also has a reflective exterior but has a hydrogel adherent surface (Probe Cover B). Probe covers will be placed on 20 premature newborns (28 to 34 weeks gestational age) following their first bath, within 24-36 hours of life. The newborns will be separated into two groups of ten each and will serve as their own controls. The first group will wear Probe Cover A. The second group will wear Probe Cover B. Probe covers will be removed on the third day of wear. Probe covers and the skin under the probe will be swabbed for bacterial growth. An exposed patch of skin opposite from the probe cover will be swabbed as a background (control) check of skin bacteria. Culture swabs will be placed in saline and serial dilutions will be made before plating onto sheep blood agar (SBA) and mannitol salt agar (MSA) plates for detection and enumeration of skin flora. Significant differences in bacterial types and amount will be noted between exposed skin and the two types of probe-covered sites. The basic parametric procedure for testing differences in groups is the T-test. The paired T-test will compare results from skin under Probe Cover A with uncovered and skin under Probe Cover B. The Mann-Whitney-U test will be used to test the difference between the two independent samples.

**Progress :** Protocol just approved by IRB and has not yet started.

## Detail Summary Sheet

**Date:** 30 Sep 95**Protocol No.:** 95/190**Status:** On-going**Title:** The Effects of Thermocouple Sensor Placement on Neonatal Skin Temperature Measurement**Start Date:** 09/15/95**Est. Completion Date:** Oct 96**Department:** Nursing**Facility:** MAMC**Principal Investigator:** Lori A. Loan, MSN, RNC**Associate Investigators:**  
Susan T. Blackburn, Ph.D.L.T. Taquino  
K. Thomas**Key Words:** Skin temperature, neonatal, thermocouple sensor placement**Accumulative****Est. Accumulative****Periodic Review:****MEDCASE Cost:** \$0.00**OMA Cost:** \$0.00

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**Study Objectives:** The objectives of this study are to compare temperature readings from probes placed on peripheral skin sites with readings of axilla temperature, and to compare temperature readings from probes placed on the abdomen and back during periods when the infant is lying -on and not lying-on the temperature probes. Also, to evaluate the effects of body size on accuracy of temperature probe measurements from selected sites, and when the infant is lying-on versus not lying-on the probe.

**Technical Approach:** This descriptive study is designed to objectively evaluate several common nursing practices and beliefs regarding the care of neonates and the placement of temperature probes. The study seek to provide a physiologic basis to support and validate nursing practice. Four body sites will be studied simultaneously through the use of a small thermocouple sensor and two channel continuous readout device. Data will be collected for one hour with the subject in each of two common positions, supine and prone. Environmental temperature and basic demographic data will also be collected for each subject and study period. The study period will consist of approximately 2.5 hours for each study subject and will not interfere with or alter the standard neonatal nursing and medical care of that infant. This study is sponsored by the local chapter of the national professional association for neonatal nursing and is designated to support data collection in multiple hospital sites. Data from all sites will be aggregated for the purpose of analysis and reporting. Descriptive statistics will be use initially to examine differences in temperature readings from the four sensors. Further analysis will examine clinically and statistically significant changes in temperature between the four sites and between lying-on and not lying-on the sensors. comparisons will also be made of differences in temperature values between sites and between infants of different weight groups.

**Progress :** Protocol just approved by IRB and has not yet started.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/076		<b>Status:</b> Terminated	
<b>Title:</b> Gastric/Jejunal Feeding[colon] Nutritional Outcomes and Pneumonia					
<b>Start Date:</b> 02/17/95			<b>Est. Completion Date:</b> Sep 96		
<b>Department:</b> Nursing			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Mary S. McCarthy, AN					
<b>Associate Investigators:</b>			LTC Bernard J. Roth, MC		
MAJ Cristopher A. Meyer, MC			2LT Faith U. Watanabe		
LTC Anthony S. Sado, MC					
<b>Key Words:</b> Feeding:gastric, Feeding:jejunal, pneumonia					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//	

**Study Objective:** 1) To compare nutritional outcome between patients randomized to gastric or jejunal tube feeders as measured by: a) daily caloric intake, b) subjective global assessment, c) biochemical parameters, d) delayed cutaneous tests and e) indirect calorimetry. 2) To compare rates of nosocomial pneumonia between gastric and jejunal fed patients as measured by: a) new & persistent infiltrate on chest x-ray (CXR), b) fever, c) sputum culture, d) leukocytosis, and e) bronchoscopically directed protected specimen brush. 3) To compare colonization rates between a subset of gastric and jejunal fed patients, at three sites (oropharynx, trachea, stomach); specific focus being Gram-negative bacilli, as measured by quantitative and qualitative microbiology analysis.

**Technical Approach:** This proposed study is a replication of a prior study done by Montecalvo et al. (Appendix A) in the medical model. Areas of interest include modifiable and non-modifiable person factors, social and physical environmental factors, physiological factors, pathophysiological factors, behavioral factors, symptoms, cognitions/emotions, and drives/sensations. Infants who are prescribed a feeding tube in one of two places, the stomach or the small intestine. Both methods are commonly used in this hospital. If you are to receive tube feedings in the stomach your doctor will pass a soft, flexible tube down your nose or mouth into your stomach. If you are to receive tube feedings in the small intestine, a radiologist will pass a soft, flexible tube down your nose or mouth using a lighted scope to guide the tube placement into your small intestine. It is the policy of this hospital to confirm the placement of the tube by xray before feedings can begin. This is ordered by the physician and will be performed whether or not you participate in this study. Shortly after having the tube in place, the principal investigator or the project director will conduct a noninvasive metabolic test at the bedside to estimate your calorie needs for tube feeding. This test measures the amount of energy you use while you are ill in the ICU. It will be performed each week. In addition, specimens of blood, urine, sputum and stomach contents will be obtained to evaluate your nutritional status and monitor for infection or bleeding. Lastly, your health record will be examined by the investigator or the project director for the following information: pertinent medical history, admission vital signs, current medications, height and weight, and tube feeding regimen.

**Progress :** This protocol was terminated due to lack of funding.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/100	<b>Status:</b> On-going
<b>Title:</b> Postoperative Wound Healing[colon] Hydration and Oxygenation		
<b>Start Date:</b> 05/06/94	<b>Est. Completion Date:</b> Oct 96	
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Brenda I. Mygrant, AN		
<b>Associate Investigators:</b> Lori A. Loan, MSN, RNC Diane M. Pierson, BS, BA, CCRN		JoAnne D. Whitney, Ph.D., RN COL Daniel G. Cavanaugh, MC
<b>Key Words:</b> wound healing:hydration, wound healing:oxygenation		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 02/17/95

**Study Objective:** 1) Compare an augmented fluid replacement protocol to a conventional fluid replacement protocol after open-heart surgery for its effects on:

a. subcutaneous tissue oxygen levels ( $p\text{SCO}_2$ ), using a subcutaneous tonometer/optode system, measured on the day of surgery and on postoperative day 1 and day 2

b. subcutaneous tissue perfusion, based on a perfusion score measured on the day of surgery and on postoperative day 1 and 2

c. wound healing indicators in wound tissue samples including: 1) hydroxyproline accumulation measured by high pressure liquid chromatography; and 2) cellular composition, fibroblast proliferation and connective tissue as measured by histologic evaluation on postoperative day 7.

2) Determine the relationships between subcutaneous tissue oxygen levels and wound healing indicators and incidence of wound complications/infections.

**Technical Approach:** This is a randomized 2 group (80 subjects per group) experimental design. Forty subjects per group will be collected in the first year, with a proposed additional 40 subjects compiled in the second year pending funding of the competitive continuation application next year. The control group will receive the standard protocol for postoperative intravenous fluid. The experimental group will receive fluid augmentation with an additional intravenous infusion of 20 cc/hr of 5% Dextrose in water (D5W). The random group assignments will be placed in envelopes that will be opened after the patient returns to the ICU from surgery, prior to the first oxygen measurement. The biochemical and cellular markers of healing will be measured 7 days postoperatively. The tissue indicators of oxygen and perfusion will be measured on the day of surgery and for the next 2 postoperative days. Sternal and leg wound assessments will be made for the first five days during hospitalization. For subjects discharged before the 7th postoperative day the ePTFE implant will be removed on the 7th postoperative day during a clinic visit. Descriptive statistics (means, standard deviation) will be used to summarize sample description variables. Student's t tests or Chi-Square analysis will be performed on the variables measured pre-intervention to ensure randomization of the two groups.

**Progress :** Thirty-one patients have enrolled in this study at MAMC in FY95. Wound healing analysis will not be done until a maximum of 50 subjects have completed the study.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/176		<b>Status:</b> On-going	
<b>Title:</b> The Effect of Perceived Social Support on the Competency Level of U.S. Army Perioperative Nursing Students					
<b>Start Date:</b> 09/15/95			<b>Est. Completion Date:</b> Mar 96		
<b>Department:</b> Nursing			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> J.E. Newman					
<b>Associate Investigators:</b>			R. Corcoran		
<b>Key Words:</b> Competency:nursing students, social support					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//	

**Study Objectives:** The purpose of this study is to determine if a relationship exists between the US Army perioperative students' perceived social support received during their 16 week course of instruction and their competency level upon completion of the course.

**Technical Approach:** The Interpersonal Relationship Inventory will be used to evaluate the student subjects' perceived social support and each perioperative course instructor will evaluate the students' competency level based on a 100 point scale (1 being worst and 100 being best). The students' competency level will be annotated on the CompetencyLevel Numeric Rating Form. Knowing the relationship between perceived social support and the competency levels in perioperative students will provide information to Army educators about the quality of social support available for perioperative students from resident staff nurses. In a profession that experiences frequent staffing shortages and position justification, it is necessary to support the education process that develops new specialists. Upon receiving returned questionnaires and subject evaluation forms, descriptive statistical analysis will be used to complete the demographic data and develop a profile of the subjects. Inferential statistics will be used to compare the selected variables. Correlational statistics will be used to demonstrate the relationship between perceived social support and competency level. The Person Product-moment correlation will be used to test that a correlation between perceived social support and competency level is different from zero, or that a relationship exists between the two variables.

**Progress :** 11 subjects have been entered, continue to accrual subjects.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/154	<b>Status:</b> Completed
<b>Title:</b> Wellness Intervention With Pregnant Soldiers		
<b>Start Date:</b> 09/21/94	<b>Est. Completion Date:</b> Sep 95	
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Judy B. Peniston, MC		
<b>Associate Investigators:</b> K.A. Lancaster Wendy M. Lombardi, DAC		
<b>Key Words:</b> pregnancy, female soldiers, wellness		
<b>Accumulative</b> <b>MEDCASE Cost:</b>	<b>Est. Accumulative</b> <b>OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objective:** The objectives of this investigation is to determine if Duraflo II, (a heparin surface treatment) creates in a controlled, prospective, randomized study, a more biocompatible extracorporeal environment as evidenced by the following key patient outcome indexes: 1) homologous transfusion requirements 2) post-op hours until extubation 3) post-op hours until SICU discharge 4) post-op days until hospital discharge.

**Technical Approach:** Cardiopulmonary bypass patients will be prospectively randomized into one of two groups. The test group will utilize cardiopulmonary bypass circuits treated with Duraflo II (surface bound USP heparin). The control group will utilize precisely the same assortment of perfusion components, but they will not have been treated with Duraflo II.

During the post-operative period the patient will have routine blood work done. Complications during the intra-operative and post-operative periods will be documented. Higgins scores will be used during the analysis of data.

**Progress :** 823 subjects were entered. Results indicated that wellness group infants had proportionately increased gestational age and birthweight; and had reduced incidence of the complications of fetal bradycardia, hyperbilirubemia, preeclampsia, and premature labor. Of clinical interest, it was discovered that the black female soldiers in this study, assessed in other studies as a highrisk group, appeared to have lower incidence of premature delivery and low birthweight when having participated in wellness intervention.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/101		<b>Status:</b> On-going	
<b>Title:</b> Fatigue Following Childbirth[colon] Military Family Outcomes					
<b>Start Date:</b> 05/06/94			<b>Est. Completion Date:</b> Sep 95		
<b>Department:</b> Nursing			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> G. Phyll					
<b>Associate Investigators:</b> M.G. Killien Karen A. Thomas, Ph.D. LTC Michelle T. Renaud, AN			Debra DePaul, RN S.T. Blackburn Lori A. Loan, MSN, RNC		
<b>Key Words:</b> childbirth:fatigue, childbirth:military					
<b>Accumulative</b> <b>MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative</b> <b>OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 09/15/95

**Study Objective:** To determine if an advanced practice nursing intervention to reduce fatigue will promote job well-being, parenting ability, and infant outcomes among military active duty personnel and their spouses/partners following the birth of an infant.

**Technical Approach:** Pregnant females and their spouses/partners (if applicable) will be recruited during weeks 28-32 of gestation in the prenatal clinic at MAMC. Data will be collected at six time points: prenatally at time of enrollment and post birth when the infant is 24-48 hours, 2 weeks, 2 months, 4 months, 6 months or age. Time measures correspond to typical timing of clinic visits. During the clinic visit, parents will complete a packet of questionnaires specific to each time of measure and active military status. If only one parent attends the clinic visit, the other parent will complete their part of the questionnaire packet at home and return it by mail. Following birth, infant neurobehavioral status will be assessed by trained study personnel at 24-48 hours of age. At 4 and 6 months of age parent-infant interaction will be assessed during the clinic visit using the NCATS observational tool. At 6 months of age infant development will be assessed by trained study personnel using the CAT/CLAMS-r and Denver II assessment instruments.

Experimental subjects will begin the fatigue modulating intervention following the initial assessment at Time 1. Throughout the study experimental subjects will receive care from the project's advanced nurse practitioners. Continuing monitoring of the intervention's integrity and effectiveness will allow the nurse practitioner to reinforce and modify the intervention as appropriate.

**Progress :** 255 subject families were enrolled. Ten families have completed the project. No data analysis has yet been done.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/115		<b>Status:</b> On-going
<b>Title:</b> Neonatal Outcomes in a Modified NICU Environment				
<b>Start Date:</b> 06/09/93			<b>Est. Completion Date:</b> Sep 94	
<b>Department:</b> Nursing			<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Michelle T. Renaud, AN				
<b>Associate Investigators:</b> Susan T. Blackburn, Ph.D.			LTC Joanna C. Beachy, MC Karen A. Thomas, Ph.D.	
<b>Key Words:</b> Neonates, modified NICU				
<b>Accumulative</b> <b>MEDCASE Cost:</b>		<b>Est. Accumulative</b> <b>OMA Cost:</b>		<b>Periodic Review:</b>
\$0.00		\$0.00		//

**Study Objective:** (1) To evaluate the effects of a modified NICU environment on physiological and neurobehavioral parameters in two groups of preterm infants and in high risk full term infants during hospitalization and post discharge; (2) to evaluate the effects of a modified NICU environment on infant-caregiver synchrony and stressors in the period of transition from hospital to home, and post-discharge.

**Technical Approach:** This is a continuation project of an ongoing study. This project extends longitudinal follow-up through the addition of a home visit and incorporates parent behavioral responses as factors relevant to infant outcomes. At the Post-Discharge Clinic Visit, 2 - 3 weeks following discharge, the mother will be asked to complete the Transition from NICU to Home Questionnaire during the infant's regularly scheduled follow-up visit. The home visit will be scheduled at the parents convenience at 82 weeks post discharge. At the home visit, the infant's neurobehavioral status will be assessed using the Brazelton Newborn Assessment Scale (BNBNS) and the infant's sleep-wake pattern will be recorded using the Newborn Child Assessment Sleep Activity (NCASA) record. Parents will complete the Parenting Stress Index (PSI) during the home visit. Parent-infant interaction during a feeding will be observed using the Nursing Child Assessment Feeding Schedule (NCASF). Home visits will be arranged to accommodate the feeding schedule.

ANOVA and repeated measures ANOVA will be used to test group differences in the BNBAS, NCAFS, PSI and Transition from NICU to Home Questionnaire. The 24-hour recordings of sleep obtained by the NCASA will be summarized and differences in total sleep and wake time, number of awakenings, and synchrony to day-night pattern will be tested using ANOVA and repeated measures ANOVA. Cyclicity of NCASA data will be determined within subject using cosinor analysis.

**Progress :** 126 subjects entered. Preliminary findings included trends toward earlier initiation of oral feedings, earlier transition to full oral feedings and slightly shorter length of stay for the experimental infants less than 37 weeks gestational age. Data analysis continues.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/074		<b>Status:</b> Terminated	
<b>Title:</b> Clinical Trial to Compare Two Tobacco Cessation Programs					
<b>Start Date:</b> 02/17/95			<b>Est. Completion Date:</b> Jan 97		
<b>Department:</b> Nursing			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Jackie W. Saye, AN					
<b>Associate Investigators:</b> MAJ Jeffrey D. Gunzenhauser, MC			Kathie J. Brendemuhl, RN		
<b>Key Words:</b> Tobacco:cessation					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> //

**Study Objective:** To compare the effectiveness of two intervention regimens on tobacco cessation rates.

**Technical Approach:** Users of tobacco products (n=360) in the Ft. Lewis and McChord Air Force Base communities will be recruited to participate in a tobacco cessation treatment program designed to target all forms of tobacco use. Potential volunteers will be screened through the use of a screening questionnaire and a limited history and physical examination. After obtaining informed consent, eligible participants will be entered into the clinical trial. Participants will be randomized to receive one of two intervention regimens. Both groups will receive an initial physician or nurse practitioner visit with advice to quit using tobacco products and prescription for nicotine replacement therapy IAW the Madigan Army Medical Center (MAMC) prescribing protocol. In addition, the first treatment group (individual phone counseling) will receive an initial face-to-face counseling session with the study nurse during which time a quit date will be selected, standardized written materials will be provided, and follow-up procedures will be reviewed; subsequently each participant in this treatment group will receive four (4) phone follow-up consultations with the study nurse at 48 hours, 1 week, 3 weeks, and 6 weeks after the preselected quit date. The second treatment group (group behavioral change course) will participate in the Madigan Tobacco Cessation Behavior Change Course, an 8-hour course, meeting as a group once a week (2 hours each session) for four weeks. During the course of the trial (1 year), participants in BOTH GROUPS will have access to the study nurse or physician by phone to address specific needs or problems. Cessation rates will be monitored by telephone interview at 3 months, following the initial interventions. Differences in cessation rates will be assessed through multivariate analysis. Determinants (confounders) of cessation other than treatment group will be included in the analytic model. Statistically significant results will be interpreted at the 0.05 level of significance.

**Progress :** Protocol terminated because it was not funded.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/065		<b>Status:</b> Terminated
<b>Title:</b> Pets as Therapy for Children During Medical Procedures				
<b>Start Date:</b> 02/17/95			<b>Est. Completion Date:</b> Oct 96	
<b>Department:</b> Nursing			<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> Ann T. Schlaefer, RN				
<b>Associate Investigators:</b> Lori A. Loan, MSN, RNC			Marjorie J. Wells, MN, ARNP LTC Richard A. Sherman, MS	
<b>Key Words:</b> Pets, therapy, children, medical procedures,Animal Study				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>	
\$0.00		\$0.00	//	

**Study Objective:** 1) To determine whether the presence of either a stuffed or live animal will result in differences over control in procedural stress responses between groups of older (8-12 years) and younger (3-7 years) children. 2) To determine what differences exist for Observation Scale of Behavioral Distress, State Anxiety Inventory for Children, pain scale, initial anticipatory fear, and actual experimental fear between the control, stuffed and live animal conditions.

**Technical Approach:** Ninety-six 3 to 12 year old subjects will be enrolled who have a cast. A brief questionnaire asking about the child's experiences with dogs in the past. At the time of cast removal, they will randomly assigned to a group which will have either a live puppy dog present for the cast removal or a group which has a stuffed puppy dog available during the cast removal. A urine sample will be taken before the cast is removed. The Project Director will place a small monitor on the child's earlobe. The blood pressure and breath count will be taken for each subject. After all the baseline information is done a stuffed animal or the live puppy dog will be brought to the subject. The animal companion will remain on the examination table with the subject during the entire cast removal. A video camera will be set up behind a curtain with the lens pointing at the subject so that his/her reactions can be recorded. These tapes will be reviewed by the Project Director at a later time to get a more accurate idea of the child's reaction to the cast removal with an animal companion. After cast removal, another blood pressure and urine sample will be collected. The parent will fill out another questionnaire. The questionnaires will be compared for differences in live dog group vs stuffed dog group using chi-square analysis. Heart rate will be analyzed using MANOVA. Pain scale will be analyzed using the Kruskal-Wallis test for the younger group, and ANOVA for the older group. Other endpoints will be descriptively analyzed.

**Progress :** Protocol terminated because it was not funded

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/033		<b>Status:</b> Completed	
<b>Title:</b> Irritable Bowel[colon] A Nursing Study of Symptoms and Coping					
<b>Start Date:</b> 11/18/94			<b>Est. Completion Date:</b> Jun 95		
<b>Department:</b> Nursing			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> M.G. Tuftin					
<b>Associate Investigators:</b> E.F. Bond P.A. Taylor			Joyce L. Tebbitt M.M. Heitkemper		
<b>Key Words:</b> bowel:irritable					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> //

**Study Objectives:** To characterize the patterning of gastro-intestinal (GI) symptoms and coping strategies in symptomatic and asymptomatic women. Also, to enhance the investigator's knowledge and skills relevant to researching clinical problems with a pathophysiological basis and symptomatology modulated by psychological and environmental stressors.

**Technical Approach:** This study will compare GI symptoms and coping strategies in 3 groups of women across 2 menstrual cycles. The three groups include Irritable bowel syndrome (IBS), IBS-like (IBSL) and asymptomatic for a total of 30 subjects. Because GI symptoms are modulated by menstrual cycle phase, diet, stress exposure and stress response, each of these potentially confounding variables will be measured. GI symptoms are measured via daily health diary; coping strategies are measured via questionnaire; menstrual phase is identified by the luteinizing hormone surge (Ovuquick), first menstruation day, and selected urinary ovarian hormone levels; diet composition is recorded in daily food records; perceived stress exposure is measured with the daily diary and other tools; stress response is measured via urinary content of stress-related hormones. Key variable will be tested for extreme deviations from normalcy. There should be no systematic difference in the variable that are collected both in the first and second menstrual cycles, unless there is an artifact caused by the testing or selection process. Nevertheless, we will test for such a systematic difference using repeated measures ANOVA with 2 within person factors, phase and cycle number.

**Progress :** 43 subjects have been entered. Results indicate no significant difference between IBS and IBSL subjects in GI symptom reports. All groups were similar in GI function. IBS and IBSL subjects were similar in psychosomatic distress levels although the IBS group score significantly higher than controls on the Global Severity Index of the SCL-90R.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/106		<b>Status:</b> On-going
<b>Title:</b> Family Home Visitation Program[colon] The Nurse as Coach				
<b>Start Date:</b> 05/07/93			<b>Est. Completion Date:</b> Jul 95	
<b>Department:</b> Nursing			<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> 1LT Barbara F. Wall, AN				
<b>Associate Investigators:</b>			Diane D. Stajduhar, RN	
Frances M. Lewis, RN, Ph.D.			Sandra L. Underhill, RN, Ph.D.	
MAJ Stacey B. Young-McCaughan, AN			MAJ Kimberly K. Armstrong, AN	
<b>Key Words:</b> Cancer: breast, home visitation				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//

**Study Objective:** (1) To test the effectiveness of a home intervention program for child-rearing families experiencing non-metastatic breast cancer in the mother; (2) to test a causal model of nurses' coaching behavior underlying the intervention; (3) to test the cost-effectiveness of the intervention.

**Technical Approach:** Subjects will be recruited whose mothers were recently diagnosed (6 months or less) with early stage breast cancer and have had either breast conserving surgery or simple modified mastectomy. Subjects will be living in a partnered relationship and have 1 or more school-age children living at home. A total of 100 families will be recruited and randomly assigned to either the Experimental or Control group.

The Experimental Group will receive home visits and the Control or Evaluation Group will receive "treatment as usual" from physicians and clinic nurses. The initial visits (by the Nurse Coach Team) will last one to one and one half hours, on 3 occasions, during which time experienced nurses will talk about the breast cancer, the concerns or issues related to it, and ways which might prove helpful in managing the experience. Each visit will include a joint session, individual sessions and a concluding joint session with the mother and partner.

The Couples' Evaluation Team Visits are made on four occasions. Each visit from that team will involve the completion of questionnaires and an interview about their experiences as a result of the breast cancer. After permission is granted the school aged children living at home will be asked to complete several questionnaires about self esteem and their relationships with their parents and friends.

The outcome analysis will employ multivariate analysis and which can detect differences between the Experimental and the Control groups.

This study will be conducted in conjunction with the University of Washington.

**Progress :** Data has been collected, but data analysis is still pending.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/078	<b>Status:</b> Completed
<b>Title:</b> The Relationship Between Skin Temperature Changes and Level of Sensory Blockade in Subarachnoid Block with Bupivacaine		
<b>Start Date:</b> 04/01/94	<b>Est. Completion Date:</b> Jul 94	
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Linda A. Webster, AN		
<b>Associate Investigators:</b> CPT Hyelan Kim, AN CPT Kyu OK Simpson, AN		
MAJ Jeffrey W. Albritton, AN CPT Michael R. Lamparelli, AN		
<b>Key Words:</b> sensory blockade, skin temperature, bupivacaine		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** To determine if skin temperature change can be used to predict the level of sensory blockade following the injection of bupivacaine into the subarachnoid space.

**Technical Approach:** This observational (n=30) study will examine changes in skin temperature as displayed on a skin temperature monitoring device concurrently with a response to a standardized "pin prick" test at dermatome levels T1 thru T10. These concurrent observations will be recorded every 2 minutes for the first ten minutes and again at fifteen minutes after the injection of bupivacaine into the subarachnoid space.

An analysis of distributions of sensory blockade lag from sympathetic blockade will be examined and numeric summary statistics will be computed. In addition to numeric techniques, graphical displays of the data will be examined to assess the individual variability and predictive usefulness of any blockade relationships found (e.g. Can skin temperature predict sensory blockade level, thereby reducing the need for repeated "pin prick" assays).

**Progress :** 29 subject were entered with no correlation being found between pinpric measurements and temperature difference. Therefore, it was concluded that skin temperature change as an indicator of sympathetic blockade cannot be used to predict sensory blockade.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/077		<b>Status:</b> Terminated	
<b>Title:</b> Wound Healing Using Pulsed Electromagnetic Field Therapy					
<b>Start Date:</b> 02/17/95			<b>Est. Completion Date:</b> Sep 96		
<b>Department:</b> Nursing			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC John B. Whittemore, AN					
<b>Associate Investigators:</b> CPT Thomas K. Curry, MC			LTC Richard A. Sherman, MS		
<b>Key Words:</b> Wounds, pulsed electromagnetic field therapy					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		//	

**Study Objective:** 1) Will pulsed electromagnetic field (PEMF) therapy increase the rate of wound healing in patients with surgical incisions left open to close by secondary intention. 2) Will PEMF therapy decrease pain management requirements in patients with surgical incisions left open to close by secondary intention.

**Technical Approach:** This is a semi-double blind, randomized, two-group experimental repeated measures design study. Subjects will initially be stratified according to their diabetes status (diabetic or non-diabetic). Following stratification, subjects will be randomized to the control or experimental group. Those subjects who are assigned to the control group will have the exact same treatment as those in the experimental group except that the PEMF machine will not be turned on during their treatment. Subjects will be randomized in blocks of 10, to insure that there will not be large imbalances between groups at any point in the study. A total of 80 subjects will be enrolled.

**Progress :** Study was terminated since study was not funded.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/145		<b>Status:</b> Completed	
<b>Title:</b> A Comparison of Smoking Cessation Behaviors Between Patients Who Have Experienced A Documented Acute Myocardial Infarction and Patients Admitted for Suspected MI					
<b>Start Date:</b> 07/01/94			<b>Est. Completion Date:</b> Dec 94		
<b>Department:</b> Nursing			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> M.E. Williams					
<b>Associate Investigators:</b>			Saptunzoff		
<b>Key Words:</b> smoking:cessation, myocarcial infarction					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		//	

**Study Objective:** To examine the differences in smoking cessation attitudes and behaviors between patients who have experienced a documented acute myocardial infarction (AMI) and patients who have been admitted to a hospital for a suspected myocardial infarction ("cardiac scare").

**Technical Approach:** A sample of 40 patients admitted with a first AMI and a sample of 40 patients admitted with suspected MI will be studied to compare the differences in smoking cessation attitudes and behaviors between the two groups. The study will be conducted using a questionnaire containing demographic questions as well as questions which seek to identify the attitudes patients have about smoking and the attitudes they have about smoking cessation. To complete the study, each participant will receive a telephone call from the investigator six weeks after his/her discharge from the hospital asking about his/her smoking status.

Demographic data will be analyzed using an unpaired t-test and chi-square analysis. A Hollingshead Four-Factor Index for socioeconomic status will be computed and correlated with reported smoking status. Mann-Whitney U test will be utilized to analyze the non-parametric data from the questionnaire and provide the statistical data to address each research question.

**Progress :** 21 subjects were entered. MI and "cardiac scare" patients exhibited similar attitudes towards smoking and smoking cessation, however, the MI group expressed a greater readiness to quit smoking 6 weeks after hospitalization.

**DETAIL SHEETS FOR PROTOCOLS**

**NUTRITION CARE DIVISION**

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/145		<b>Status:</b> Completed	
<b>Title:</b> Field Test of Practice Guidelines for Nutrition Care of Type I Insulin Dependent Diabetes Mellitus					
<b>Start Date:</b> 06/16/95			<b>Est. Completion Date:</b> Jul 95		
<b>Department:</b> Nutritution Care Division			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> M.J. Endler					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Diabetes:nutrition					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		//	

**Study Objective:** To determine if the implementation of recently developed nutrition practice guidelines for Type I, insulin dependent diabetes mellitus (IDDM) positively affects patient outcomes compared to usual care.

**Technical Approach:** This is a multicenter study. Five to 10 Type I diabetes mellitus patients seen in the MAMC Nutrition Clinic will be asked to participate. Institutions will be randomly assigned to control (usual care) or intervention (new guideline) groups. MAMC has been randomly chosen to enter patients in the control group. The differences from usual care are (1) the subjects will have blood glucose levels taken at the beginning and end of the three month study period; and (2) subjects will be asked to fill out a brief questionnaire about their health and perceptions of nutrition care at the end of the three month study period.

**Progress :** 2 subjects were entered at MAMC. Data analysis is still pending.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF OBSTETRICS/GYNECOLOGY**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/011	<b>Status:</b> Suspended
<b>Title:</b> The Incidence of Spontaneous Abortion in Obese Patients[colon] A Retrospective Chart Review		
<b>Start Date:</b> 09/02/94	<b>Est. Completion Date:</b> Jun 94	
<b>Department:</b> Obstetrics/Gynecology	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Karen E. Hayes, MC		
<b>Associate Investigators:</b> CPT David H. Harrison, MC MAJ Alicia Y. Armstrong		
<b>Key Words:</b> Abortion, obesity		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** To determine the response rates of metastatic or locally advanced breast cancer with administration of four cycles of high doses of Taxol as a three hour infusion with Rhu-G-CSF support. 2) To evaluate the feasibility of administering this regimen for at least four cycles.

**Technical Approach:** Women with metastatic Stage IV or locally advanced Stage IIIb breast cancer, with measurable disease, will be eligible for this study. Although patients may have received adjuvant chemotherapy, they should not have received any chemotherapy for metastatic disease. All patients will receive a premedication regimen prior to taxol administration. Taxol will be administered as a three hour continuous infusion at a dose of 250 mg/m<sup>2</sup>; the infusion will be repeated every 3 weeks. Rhu-G-CSF will be given at 5 ug/kg subcutaneously from day 2 of every cycle. After completion of the four cycles, further treatment, including continuation of Taxol will be at the discretion of the investigator.

**Progress :** No information could be located, nor could the old PI be contacted.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/129		<b>Status:</b> On-going	
<b>Title:</b> The Non-invasive Detection and Characterization of Anal Incontinence in the Parous Female Population					
<b>Start Date:</b> 06/16/95			<b>Est. Completion Date:</b>		
<b>Department:</b> Obstetrics/Gynecology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL Gary D. Davis, MC					
<b>Associate Investigators:</b> C.S. Beverly			B.G. Bute P.L. Mallory		
<b>Key Words:</b> Incontinence:anal, pregnancy					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		//

**Study Objectives:** This study attempts to determine the frequency and nature of obstetric-related anal incontinence by using non-invasive techniques. Anal sphincter and pudendal nerve status would be assessed and correlated with patient questionnaire complaints and manometric measurement of function.

**Technical Approach:** Permanent anal incontinence is reported to complicate 4-6 percent of vaginal deliveries and has been blamed on pudendal nerve injury or sphincter muscle damage. A non-invasive study of 300 pregnant women during and after pregnancy is proposed to attempt to differentiate between neuronal, muscular or combination injuries which produce incontinence. Volunteer subjects would be assessed for: pudendal nerve terminal motor latency as a measure of innervation, manometric variables as an indicator of function and transanal ultrasound as a morphologic study. Comparison of results before and after delivery would help determine the cause of obstetric-related anal incontinence. Standardized anorectal physiology data would be recorded for each patient to include resting pressure, maximal squeeze pressure, presence of rectoanoinhibitory reflex, sphincter length, and sensory threshold. Statistical analysis will evaluate for differences being due to chance with less than five percent being considered significant ( $p \leq 0.05$ ). Tests for ordinate and continuous variables will be employed as appropriate.

**Progress :** Awaiting grant funding from MRMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/083		<b>Status:</b> Completed	
<b>Title:</b> A Randomized Trial of Low Dose Aspirin in Pregnancies with Unexplained Elevations of Maternal Serum Alpha-Fetoprotein					
<b>Start Date:</b> 04/02/93			<b>Est. Completion Date:</b> Jun 94		
<b>Department:</b> Obstetrics/Gynecology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Katherine S. Foley, MC					
<b>Associate Investigators:</b> LTC Arthur S. Maslow, MC COL John A. Read II, MC			MAJ Timothy J. Boley, MC MAJ Jerome N. Kopelman, MC MAJ Glenn R. Markenson, MC		
<b>Key Words:</b> alpha-fetoprotein:low dose aspirin					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		//

**Study Objective:** 1. To determine if pregnancies with unexplained elevated maternal serum alpha-fetoprotein (MSAFP) would benefit from low dose aspirin therapy. 2. To determine the association between unexplained elevations in MSAFP and antiphospholipid antibodies (APA) and antinuclear antibodies (ANA). 3. To compare placental pathology in those patients with unexplained elevated MSAFP treated with aspirin and with no treatment.

**Technical Approach:** All patients with unexplained elevated MSAFP, greater than 2.0 multiples of the median, and no history of prior perinatal morbidity or mortality, will be offered entry into the study. All patients will be screened for the presence of autoantibodies, specifically anticardiolipin antibodies, and lupus anticoagulant and antinuclear antibodies. The participants will then be randomized into four groups as follows: Group 1-Unexplained elevated MSAFP with absence of antiphospholipid antibodies, treated with low-dose aspirin. Group 2-Unexplained elevated MSAFP with absence of antiphospholipid antibodies, treated with placebo. Group 3-Unexplained elevated MSAFP with the presence of antiphospholipid antibodies, treated with low-dose aspirin. Group 4D: Unexplained elevated MSAFP with the presence of antiphospholipid antibodies treated with placebo. All patients will be followed in the Complicated Obstetrical Clinic and will receive serial ultrasounds to assess fetal growth. Antepartum fetal testing will consist of biweekly non-stress tests and weekly amniotic fluid indices. Also, uterine artery blood velocity waveform indices will be obtained at initial entry into the study, at 24 - 28 and 32 - 36 weeks gestational age. In addition, all placentas will be sent to pathology for a histologic examination. Students t-test will be used for measured items such as newborn weights, amniotic fluid volume, and Doppler flow systolic/diastolic ratios. Statistical analysis of the grading of chronic villitis will employ the non-parametric Mann-Whitney U test. Categorical items, such as mode of delivery, preeclampsia, abruptions, presence of autoantibodies, non-reactive non-stress tests, pre-term delivery, and pre-term labor, will be analyzed using the chi-square technique.

**Progress :** Ten subjects have been enrolled in this study in FY95. Data analysis is being done by Dr. Glenn Markenson at TAMC.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 92/101		<b>Status:</b> On-going	
<b>Title:</b> Neurodevelopmental Follow-Up of Infants of Mothers Who Seroconvert to HSV During Pregnancy					
<b>Start Date:</b> 09/04/92			<b>Est. Completion Date:</b> Mar 94		
<b>Department:</b> Obstetrics/Gynecology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Roderick T. Hume JR, MC					
<b>Associate Investigators:</b> LTC Glenn C. Tripp, MC			Millie Herd, AN MAJ Jerome N. Kopelman, MC		
<b>Key Words:</b> herpes simplex virus, pregnancy					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//	

**Study Objective:** To evaluate infants of sero-converters by means of Denver Developmental Tests and type specific HSV antibodies by Western blot in order to answer the following questions: does maternal HSV-2 seroconversion during pregnancy without evidence of asymptomatic shedding of the virus from the genital tract at the onset of labor or evidence of acute neonatal HSV infection result in significant neurodevelopmental disability in the offspring; and can asymptomatic HSV seroconversion in the newborn occur as a result of in utero infection or undetected perinatal transmission without evidence of acute neonatal infection.

**Technical Approach:** About 3% of women who are HSV seronegative at the first prenatal visit are HSV seropositive at the time of delivery. If the maternal HSV cultures were negative on admission to the labor suite and the neonatal conjunctival and nasopharyngeal cultures were negative on day 2 of life, the newborns are discharged from the hospital at 1-5 days postpartum. The only long term follow-up performed has been routine pediatric care. However, any long term neurodevelopmental consequences to the uninfected offspring of women experiencing an asymptomatic first episode of genital HSV during pregnancy are unknown. This study will be done in conjunction with Children's Hospital, Seattle, WA, and the University of Washington. Approximately 20 children will be studied at Madigan. At six months of age, the child will be administered the modified Denver Developmental Test, and a blood sample will be drawn to measure type-specific HSV antibodies by Western blot. By six months of age, passively acquired maternal antibody should be completely metabolized. HSV antibody present at this time should represent an asymptomatic congenital or neonatal infection and seroconversion. Information regarding the mother's demographic profile and pregnancy history, her serologic and virologic profiles, and the infant data (e.g., birth weight, gestational age) will also be obtained.

**Progress :** 878 subjects entered. Seroconversion during pregnancy but before the onset of labor was associated with an increase in asymptomatic HSV shedding at the onset of labor but no discernible effect on pregnancy outcome and no neonatal transmission. In contrast, HSV seroconversion occurring at the onset of labor was associated with a high rate of neonatal transmission.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/138		<b>Status:</b> Suspended	
<b>Title:</b> Once vs Thrice Daily Gentamicin Dosing in Postpartum Endomyometritis					
<b>Start Date:</b> 08/05/94			<b>Est. Completion Date:</b>		
<b>Department:</b> Obstetrics/Gynecology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> S.M. Kambiss					
<b>Associate Investigators:</b> CPT Anne B. Shrout, MC			MAJ Jerome N. Kopelman, MC		
<b>Key Words:</b> endomyometritis, gentamicin, dosing					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		//	

Study Objective: To evaluate the once-daily dosing of gentamicin compared to the usual thrice-daily regimen of gentamicin in the treatment of postpartum endomyometritis and in patients with chorioamnionitis that undergo cesarean section.

Technical Approach: Patients will be enrolled from the patient population at Madigan. They must be diagnosed with postpartum endomyometritis or with chorioamnionitis and subsequent cesarean section. Patients will be randomized into two arms. Group 1 will receive the standard gentamycin 1.75 mg/kg every 8 hours IVPB with clindamycin 900 mg every eight hours. Group 2 will receive gentamycin 5.25 mg/kg every 24 hours IVPB and clincamycin 900 mg every eight hours IVPB. Both groups will have frequent drug levels obtained from a heplock in the opposite arm. All patients will remain on antibiotics until afebrile X 48 hours. Clinical response and failure will be determined by chi-square.

Progress : Original PI (Dr. Shrout) PCS'd in July 1995 after entering 8 patients. The protocol has been suspended because DCI has been unable to get a report from Dr. Kambiss.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/155		<b>Status:</b> Terminated
<b>Title:</b> Pregnancy Outcomes Comparison Between Active Duty Military Women and Working and Non-working Family Members				
<b>Start Date:</b> 09/21/94		<b>Est. Completion Date:</b> Sep 95		
<b>Department:</b> Obstetrics/Gynecology		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Wendy M. Lombardi, DAC				
<b>Associate Investigators:</b>		LTC Roderick T. Hume JR, MC		
<b>Key Words:</b> Pregnancy:outcomes, female soldiers				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//

**Study Objective:** To evaluate the differences between the pregnancy outcomes of active duty soldiers, working family members, and non-working family members.

**Technical Approach:** This study entails tracking pregnancy outcomes at MAMC and comparing those outcomes between active duty soldiers and working family members and non-working family members. Data will be gathered from an initial questionnaire, mid-pregnancy questionnaire (5 1/2 - 6 1/2 months gestation), and obstetric and delivery records. Through this series of questionnaires and surveys demographic information will be obtained. Additionally, information will be collected regarding an individuals' type and quantity of work, stress levels at work, other kinds of physical activity in which they engage, lifestyle and social habits, and self esteem and morale. These can be considered variables which may affect pregnancy outcomes and/or complications.

Data collection from obstetric and delivery records will include types of complications, method of delivery, labor duration, gestational age and infant weight at birth, NICU stay (if applicable), and the costs related to the delivery and/or neonatal care. Dependent variables will be pregnancy outcomes (birth weight, gestational age at delivery, Apgar score) and complications; Independent variables will be type and quantity of work, perceived stress levels, lifestyle and social habits and self esteem.

**Progress :** Grant was approved for funding, but post APFT standard policy changed, thereby making the study impossible, so grant was withdrawn prior to initiation.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/159		<b>Status:</b> On-going	
<b>Title:</b> Three Dimensional Ultrasound					
<b>Start Date:</b> 07/21/95			<b>Est. Completion Date:</b> Jun 96		
<b>Department:</b> Obstetrics/Gynecology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Christian R. Macedonia, MC					
<b>Associate Investigators:</b> MAJ Jerome N. Kopelman, MC COL Dan C. Moore, MC			LTC Arthur S. Maslow, MC Troy H. Patience, B.S.		
<b>Key Words:</b> Ultrasound, 3D					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//	

**Study Objective:** To assess the feasibility and quality of three dimensional reconstruction of conventional two-dimensional ultrasound images using a low-cost and transportable system.

**Technical Approach:** We propose to use a continuous running acquisition process for three dimensional ultrasonographic data visualization. The process involves the use of a worm drive linear translation device coupled to a conventional two-dimensional ultrasound transducer. this transducer sends conventional 2 dimensional ultrasonographic data streams to a standard 2D image processor. The RGB output from that processor is downloaded into a 3D graphics workstation where it is rendered into a three dimensional image. This image can then be manipulated to provide novel views of internal anatomy. It can also be used to make size and weight estimations of internal organs for preoperative planning.

**Progress :** This is a new protocol. Waiting for approval from CIRO.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/070		<b>Status:</b> Completed	
<b>Title:</b> The Effect of Nicotine and Cigarette Smoke Extract on Endothelium-Derived Vasoactive Substances Produced in the Doubly Perfused Placental Cotyledon Model					
<b>Start Date:</b> 03/05/93			<b>Est. Completion Date:</b>		
<b>Department:</b> Obstetrics/Gynecology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Glenn R. Markenson, MC					
<b>Associate Investigators:</b>					
LTC Arthur S. Maslow, MC			MAJ Timothy J. Boley, MC		
COL John A. Read II, MC			MAJ Jerome N. Kopelman, MC		
<b>Key Words:</b> cotyledon:placental, nictotine					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		//	

**Study Objective:** Evaluate the effects of nicotine and cigarette smoke extract on the production and release of prostacyclin, thromboxane, nitric oxide and Endothelin 1 by the dually perfused placental cotyledon model.

**Technical Approach:** Nicotine and cigarette smoke extract will be added to the standard perfusate during a two hour period as described previously (Protocol 92/71). The establishment of the doubly perfused, placental cotyledon model for the in vitro investigation of the umbilical-placental circulation). This solution will then be used to perfuse the cotyledon model to see the effect that these compounds have on the vasoactive substances produced by the model. The viability of the system will be monitored by glucose consumption, potassium levels, and oxygen consumption. Perfusion pressure and pH will also be monitored.

The effluents from the paternal and fetal circulations will be sampled every 15 minutes during the nicotine/cigarette smoke extract infusion. These samples will be analyzed for levels of nicotine, cotinine, nitric oxide, thromboxane (TXB2), 6-keto-PGF1 (stable metabolite of prostacyclin) and Endothelin 1.

Statistical analysis will be performed using the t-test and ANOVA.

**Progress :** Twenty cotyledons from ten placentas (five smokers and five nonsmokers) were perfused. In the fetal circulation, pre-treatment TBX2 levels were significantly higher in cotyledons from smokers than in nonsmokers. In the intervillous circulation, TBX2 tended to be higher in cotyledons from smokers versus nonsmokers but this difference was not significant. There was no change in TBX2 levels after the addition of nicotine in any of the cotyledons. Cigarette smoking during pregnancy may affect fetoplacental circulation by causing an increase of thromboxane in the placenta. Nicotine did not have an effect on the levels of thromboxane or prostacyclin in our model.

### Detail Summary Sheet

**Date:** 30 Sep 95      **Protocol No.:** 95/112      **Status:** Completed

**Title:** Influence of Parenteral Progesterone Administration on the Prevalence and Severity of Mastodynia in Active Duty Servicewomen. A Multi-institutional Case-Control Study

**Start Date:** 04/21/95      **Est. Completion Date:** Apr 96

**Department:** Obstetrics/Gynecology      **Facility:** MAMC

**Principal Investigator:** MAJ Mary C. Nace, MC

<b>Associate Investigators:</b>	D.M. Euhus
M. Mirto	C. Uyehara
H. Kailani	S. Stachecki
C. Howley-Bowland	M. Munns
H.J. Bartell	S. Dunlow
J. Turek	J. Anderson

**Key Words:** Mastodynia, preogesterone

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	//

**Study Objectives:** To assess the efficacy of progesterones in the prevention and treatment of mastodynia. To determine the prevalence and quantitate the severity of mastodynia among active duty service women. To quantitate the impact of mastodynia on productivity and military readiness. To assess whether health care providers are meeting the expectations of women with mastodynia.

**Technical Approach:** This study proposes to address the objectives by polling 6% of active duty service women in the U.S. between the ages of 18 and 44 to determine the frequency of breast pain and estimate the impact on military readiness. A questionnaire will be used to document the presence and measure the severity of breast pain. A cross-sectional method will be used to compare the frequency of mastodynia between women receiving long term progesterone supplementation (as contraception) and those not receiving supplementation. This will provide information on the effectiveness of continuous progesterone supplementation on the prevention and/or treatment of mastodynia. A positive result would influence the treatment recommendations for pre-menopausal women suffering from mastodynia. Women with breast pain will be asked how they feel about the quality of the evaluation and treatment they received. This will help direct and focus future educational efforts to improve health care for women in the military. Statistical measures will include Fischer's Exact Test for validation of the study questionnaire, Descriptive studies to characterize mastodynia in active duty women, and Logistic Regression to study the influence of continuous parenteral progesterones on the prevalence of mastodynia.

**Progress :** None of the investigators could be located for study results.

### Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 94/085

**Status:** On-going

**Title:** Operative Endoscopy and Surgical Management of the Bowel and Urinary Tract Injuries in Gynecologic Surgery in the Pig (*Sus scrofa*) and Goat (*Capri hircus*)

**Start Date:** 02/09/94

**Est. Completion Date:** Feb 97

**Department:** Obstetrics/Gynecology

**Facility:** MAMC

**Principal Investigator:** LTC Mark E. Potter, MC

**Associate Investigators:**

D.M. Magelssen

MAJ Alicia Y. Armstrong

COL Paul N. Smith, MC

MAJ Rosemary L. Casey, MC

MAJ Mary C. Nace, MC

**Key Words:** Surgical management:gynecology, endoscopy, pig, goat,Animal Study

**Accumulative**

**MEDCASE Cost:** \$0.00

**Est. Accumulative**

**OMA Cost:** \$0.00

**Periodic Review:**

//

**Study Objective:** 1) To familiarize residents in OB/GYN with techniques of management of bowel and urinary tract injury with suturing or stapling techniques. 2) To familiarize residents with techniques for colostomy, ileostomy, ureteroneocystostomy and vascular injury repair. 3) To expand the operative endoscopy experience of OB/GYN Residents and Staff, prior to utilization in humans.

**Technical Approach:** With the animal in the supine position, a midline incision will enter the abdomen and repair of lacerations and anastomosis will be performed by standard techniques. Additional surgical procedures may include ureteroneocystostomy. The abdomen will be closed. A second episode of surgery will occur 3-4 weeks later and additional procedures including colostomy, loop ileostomy, and vascular injury repair will be carried out. Following the second surgical episode, the animal will not be allowed to recover from anesthesia. In some cases an animal may be used for a single training episode. When this occurs, euthanasia will be carried out at the completion of the session. When follow-up evaluation of a surgical procedure is desired, no more than one procedure will be done on that animal during the first episode. The animal will then be allowed to recover and will be re-anesthetized and reoperated 3-4 weeks later. During the second surgical episode, more than one procedure may be performed. The animal will be euthanized at the end of the episode while still under general anesthesia. Procedures which would normally involve any postoperative care beyond normal husbandry will only be performed during the last surgical episode to which that particular animal is subjected. The animal will be euthanized while still under general anesthesia.

**Progress :** No sessions were held in FY 95.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF PATHOLOGY**



### Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 95/117

**Status:** On-going

**Title:** Investigation of Morphologic Features of Atypical Squamous Cells on PAP Smears with Human Papilloma Virus DNA Probe Correlation

**Start Date:** 06/16/95

**Est. Completion Date:** Jun 96

**Department:** Pathology

**Facility:** MAMC

**Principal Investigator:** MAJ Barbara A. Crothers, MC

**Associate Investigators:**

CPT Daniel D. Mais, MC

**Key Words:** Human papilloma virus, DNA, PAP, morphologic features

**Accumulative**

**Est. Accumulative**

**Periodic Review:**

**MEDCASE Cost:** \$0.00

**OMA Cost:** \$0.00

//

**Study Objective:** To test the hypothesis that there are defined morphologic features of "Atypical Squamous Cells of Uncertain Significance (ASCUS), suggestive of Low Grade Squamous Intraepithelial Lesion (LGSIL)" which differ significantly from reactive changes on the cervicovaginal PAP smear and can be used to predict the presence of the Human Papilloma Virus (HPV).

**Technical Approach:** This study will consider a group of 250 female patients, all with PAP smears reported as "atypical squamous cells (ASCUS)" or "reactive changes" from 1 July 1993 to 1 July 1994. The PAP smears will be evaluated independently by the two investigators for the presence or absence of certain predefined morphologic features. These results will be tabulated. All of the PAP smears will then be subjected to DNA probes by *in situ* hybridization (ISH), testing for the presence of HPV types 6, 11, 16, 18, 31 and 33. Cases which reveal viral DNA within the observed atypical cell will be considered positive and all others will be considered negative for LGSIL. The accumulated morphologic data will be subjected to multivariant statistical analysis to determine the significance of each feature in predicting the presence of HPV. The investigators will attempt to establish which features are most useful as criteria for reclassifying ASCUS PAP smears as LGSIL.

**Progress :** Project is on hold pending a method to fund this project.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF PEDIATRICS**

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/052		<b>Status:</b> On-going	
<b>Title:</b> Intrauterine Growth[colon] Factors That Influence the Relationship Between Gestational Age and Birth Weight, Length, and Head Circumference					
<b>Start Date:</b> 03/05/93			<b>Est. Completion Date:</b> Mar 96		
<b>Department:</b> Pediatrics			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Joanna C. Beachy, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> intrauterine growth, age, birthweight, length, head circumference					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$1000.00		//	

**Study Objective:** (1) How does the relationship between gestational age and birth weight, length, and head circumference from data gathered from newborn infants compare with published data? (2) Does the average birth weight, length, head circumference and ponderal index at each gestational age differ from year to year of the study (1981 - 1992)? (3) Do infants from twin/multiple gestation pregnancies in this selected population show the expected growth pattern, that is no alteration in growth until the third trimester? (4) Does the classification of diabetic (gestational versus non-gestational) impact on incidence of large for gestational age infants and on the ponderal index?

**Technical Approach:** This is a retrospective review of data from > 24,000 infants born over an 11 year period. Infants with diagnosed congenital anomalies, chromosomal abnormalities and hydrops fetalis will be excluded.

**Data Analysis:** 1) For evaluation of effect of gestational age on birth weight, length, head circumference and ponderal index, all multiple gestation infants and IDMs will be excluded. Data will be analyzed by non-linear regression to generate curve with 95% confidence levels. Alternatively, mean ( $\pm 2$ ) standard deviations, third and tenth percentile of birth weight, length and head circumference will be calculated for each gestational age. A smoothed curve will then be generated and compared to previously published curves. 2) Data will also be stratified by year and analyzed in a similar fashion, that is birth weight, length and head circumference will be compared at each gestational age yearly from 1981 - 1992. Statistical significance will be evaluated by regression analysis or ANOVA, controlled for gestational age. 3) The birth weight, length, head circumference and ponderal index from infants of multiple gestations will be evaluated as in (1) and compared with the standard curves generated in (1) and published for twin gestations. Evaluation of the ponderal index may indicate when the placental supply is no longer sufficient. 4) The birth weight, length, head circumference and ponderal index from IDM will be handled in a similar manner. Subdivision of data by White's category of maternal diabetes will be done.

**Progress :** Data collected and entered on 16,893 births, data analysis is about ready to be started.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 90/058		<b>Status:</b> Terminated	
<b>Title:</b> Neonatal Emergency Procedure Training in the Rabbit Model					
<b>Start Date:</b> 04/20/90			<b>Est. Completion Date:</b> Indef.		
<b>Department:</b> Pediatrics			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Joanna C. Beachy, MC					
<b>Associate Investigators:</b>			LTC Matthew M. Rice, MC		
<b>Key Words:</b> training protocol,neonatal,rabbit,neonatal emergency procedure,Animal Study					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$864.00	06/10/94	

**Study Objective:** To train physicians who have not been previously trained in emergency management of neonates who will be called upon to perform this function in the Neonatal Intensive Care Unit.

**Technical Approach:** This training is designed for junior house staff who are inexperienced in the management and emergency care of sick infants. Demonstration by a staff neonatologist of the various procedures to be learned will be performed before any hands on attempts by the interns and residents. The animal lab will allow the student to observe and practice to proficiency those lifesaving skills necessary in the management and stabilization of the neonatal patient. Telazol, 15 mg/kg, and xylazine, 5 mg/kg IM, will be administered to induce and maintain anesthesia. Additional anesthesia will be administered in increments as needed. The rabbits will be intubated with a 2-3 mm id endotracheal tube and ventilation will be maintained as necessary with 100% oxygen. Tracheal intubation, venous cutdown, needle thoracocentesis, and chest tube insertion will be performed by each intern or resident in attendance.

**Progress :** No animals were used in FY 95. A revised protocol was not presented for review for continuation. The protocol was terminated after being open for over 3 years.

## Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 91/055

**Status:** Terminated

**Title:** Use of the Children's Yale Brown Obsessive Compulsive Scale (CY-BOCS) Symptom Checklist as an Initial screening Interview for Identification of Obsessive Compulsive Disorder (OCD) and Related .....

**Start Date:** 04/05/91

**Est. Completion Date:**

**Department:** Pediatrics

**Facility:** MAMC

**Principal Investigator:** MAJ Robert B. Broadhurst, MC

**Associate Investigators:**  
Jennifer S. Achilles

LTC Patrick C. Kelly, MC

**Key Words:** OCD, screening, Yale Brown Compulsive Scale, symptom checklist, children: 7 - 18 YO

**Accumulative**

**Est. Accumulative**

**Periodic Review:**

**MEDCASE Cost:** \$0.00

**OMA Cost:** \$0.00

//

**Study Objective:** To determine if the short interview is a clinically useful format for identifying Obsessive Compulsive Disorder (OCD) in childhood and to further evaluate the diagnostic screening properties of the CY-BOCS as a semi-structured interview looking for OCD in childhood.

**Technical Approach:** Approximately 1000 subjects will be selected for interviewing. This will consist of 500 subjects 7 to 12 years old and 500 subjects 13 to 18 years old. Subjects will be randomly selected from appointment rosters. While the parent(s) and child are waiting in the waiting room, they will be asked about participating in this protocol. We will explain that this will involve a 10 minute interview of parent(s) and child in a private exam room. Using the chi-square test, comparisons will be made between the positive and negative short interview groups, between the positive and negative CY-BOCS interview groups, between the positive and negative physical exam finding groups, between the positive trichotillomania/eating behavior and negative groups. Concordance of all positive groups will be assessed. Demographic data in positive and negative groups will be compared. From analysis of the above groups, information on the selectivity of the short interview versus the CY-BOCS for OCD diagnosis at follow-up will be formulated. Minimal prevalence rates of OCD will be assessed for this clinic sample. All positive interview groups and physical exam findings will be compared with diagnoses and medical problems at follow-up evaluation. All diagnoses and medical problems will be determined at follow-up interview, as the gold standard for establishing any diagnosis or medical problem in this study. Data in all the negative groups will be assessed for frequency of "1" level symptoms, trichotillomania symptoms, and eating disorder symptoms on the CY-BOCS according to age, sex and sponsor rank. This will also be correlated with any later DSM diagnoses, which may come about on follow-up clinical interviews.

**Progress :** No subjects were enrolled in FY95. The protocol was terminated after failure to find a new PI.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/137		<b>Status:</b> On-going	
<b>Title:</b> The Relationship of Positive Skin Tests to House Dust Mite, Grass Pollen, and Cat Dander to Asthma in Children Presenting to a Pediatric Pulmonary Clinic					
<b>Start Date:</b> 06/16/95			<b>Est. Completion Date:</b> Sep 96		
<b>Department:</b> Pediatrics			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Edward R. Carter, MC					
<b>Associate Investigators:</b> J.W. Delaney Troy H. Patience, B.S.			E.J. Matheson COL Donald R. Moffitt, MC		
<b>Key Words:</b> Asthmadust mite, grass pollen, can dander, minors					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		//	

**Study Objectives:** To determine the following in children who attend the MAMC Pediatric Pulmonary Clinic: (1) the prevalence of positive skin tests to house dust mite (2 species), cat dander, and grass pollen in children with asthma  $\geq 4$  years old; (2) whether there is positive correlation between severity and chronicity of asthma and positive skin tests, especially to house dust mites; (3) whether there is positive correlation between the age of the child with asthma and the probability of having a positive skin test; (4) whether there is positive correlation between signs/symptoms of allergy and positive skin tests, especially to house dust mites in children with asthma; (5) relationships between total serum IgE, blood eosinophilia, asthma, and allergy in asthmatic patients and to establish the predictive value of these serologic tests for skin test positivity in asthmatics; and (6) to devise an algorithm for deciding which children need an allergy referral, which children should undergo environmental controls without a formal allergy assessment, and which children have such a low risk for allergy that no allergy assessment is necessary.

**Technical Approach:** A total of 100 to 200 children  $\geq 4$  years old with asthma presenting to the MAMC Pediatric Pulmonary Clinic for evaluation will be asked to participate in this observational study. Children who meet the diagnostic criteria for asthma will be eligible. Severity of asthma will be categorized as mild, moderate, or severe, based upon test criteria. Asthma will also be categorized as chronic or intermittent based upon the frequency of signs /symptoms. We will make all attempts to include consecutive children to ensure a representative sample. Subjects will complete a questionnaire and a complete history and physical will be performed. Blood will be drawn for serum IgE and peripheral blood eosinophil determination. They will receive skin prick tests for sensitivity to house dust mite, grass pollen, cat dander and 2 controls. We will determine the frequency of positive skin tests in this sample and assess the relationships between positive skin tests and patient age, severity and chronicity of asthma, signs/symptoms of allergy, an elevated serum total IgE, and blood eosinophilia. Data analysis methods will include chi-square for presence or absence of an effect on positive skin test for each variable. Multiple regressions will be performed for positive skin tests as a whole and then individually for each of the 3 specific skin tests. These regression analyses will determine which variables or combination of variables that best predicts a positive skin test in these asthmatic children.

**Progress :** Approximately 55 subjects entered to date. Still in the process of collecting data. Study is progressing smoothly.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/098		<b>Status:</b> Completed	
<b>Title:</b> Is the Use of Nose Clips Necessary in Children Performing Routine Spirometry?					
<b>Start Date:</b> 05/06/94			<b>Est. Completion Date:</b> Sep 94		
<b>Department:</b> Pediatrics			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Edward R. Carter, MC					
<b>Associate Investigators:</b> M. Berhens			COL Donald R. Moffitt, MC		
<b>Key Words:</b> Spirometry:children, nose clips					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//	

**Study Objective:** To determine whether the use of nose clips significantly affects spirometric values in children performing routine spirometry.

**Technical Approach:** This is a randomized, investigator-blinded, prospective, crossover study that will involve 100 subjects. Each subject will be asked to perform spirometry without nose clips and then again with nose clips. Half will be randomized to perform spirometry without nose clips first and the other half will perform spirometry first with nose clips. The investigator involved with the pulmonary function testing will not know when the nose clips are being used. Each subject will perform a minimum of three acceptable spirometric maneuvers with and without nose clips. Standard pulmonary function values will be obtained.

Patients will be placed into 4 groups of children:  $\leq 10$  years-old and who have never performed spirometry (Group 1);  $\leq 10$  years-old who have performed spirometry in the past (Group 2);  $> 10$  years-old have never performed spirometry (Group 3); and  $> 10$  years-old who have performed spirometry before. Groups were chosen because both experience with the test and the age of the patient may influence the affect of nose clips on spirometry.

**Progress :** 81 subjects entered. Completed data collection. Combined data from children with the adult data. In 1995 we completed data collection, analyzed the data, and submitted a manuscript for publication We found that the use of nose clips did not affect spirometric values. We concluded that the use of nose clips was not necessary in children when performing routine spirometry.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/041		<b>Status:</b> Terminated	
<b>Title:</b> The Short-Term Use of a Helium-Oxygen Mixture in Infants Hospitalized With Bronchiolitis					
<b>Start Date:</b> 12/04/92			<b>Est. Completion Date:</b> May 93		
<b>Department:</b> Pediatrics			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Edward R. Carter, MC					
<b>Associate Investigators:</b> CPT Anthony R. Neri, MC			COL Donald R. Moffitt, MC		
<b>Key Words:</b> bronchiolitis: helium-oxygen, infants					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$1258.72		//	

**Study Objective:** To determine if the inhalation of a 30% oxygen - 70% helium mixture (heliox) will improve the ventilation and clinical status of infants hospitalized with bronchiolitis.

**Technical Approach:** Patients will be stabilized and placed in a special plastic box which is placed over the head and chest into which oxygen enriched air can be placed. Baseline measurements will be recorded with the patient breathing 30% oxygen. The patient will then be randomized to receive first either heliox or enriched air with a fractional inspired oxygen concentration ( $\text{FIO}_2$ ) of 30%. Measurements will be taken at baseline and then 10 minutes after breathing the first gas mixture. The subject will then receive the second gas mixture and measurements recorded again in 10 minutes. The primary measurements will be respiratory rate, a clinical score adapted from an established clinical scoring system for bronchiolitis, heart rate, oxygen saturation, and transcutaneous partial pressure of carbon dioxide ( $\text{TcPCO}_2$ ). If an arterial line has been placed for clinical reasons we will also measure the partial pressure of carbon dioxide in arterial blood ( $\text{PaCO}_2$ ).

Primary end points are changes in  $\text{PCO}_2$  (transcutaneous and possibly arterial), clinical score, respiratory rate and heart rate. Differences between continuous variables will be analyzed with the two tailed Student's t test, and differences in clinical score (median) will be assessed with the Wilcoxon rank sum test.

**Progress :** 3 subjects entered. Nothing was done on this protocol during FY 95. The outcome variables were too difficult to assess. The study was terminated.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/129		<b>Status:</b> On-going	
<b>Title:</b> Randomized Trial of Nerbulized vs Instilled Cromolyn Sodijm (Intal) in the Preventin of Airway Inflammation in Ventillated Premature Neonates					
<b>Start Date:</b> 07/02/93			<b>Est. Completion Date:</b> May 94		
<b>Department:</b> Pediatrics			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Thomas D. Carver, MC					
<b>Associate Investigators:</b> MAJ Margaret G. Richardson, MS LTC Deborah J. Leander, AN			CPT Katherine M. Hermann, MC LTC Robington J. O. Woods, MC		
<b>Key Words:</b> Neonates: airway disease, cromolyn sodium, Intal,					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$4379.00		10/21/94	

**Study Objective:** To evaluate the efficacy of direct intra-tracheal instillation of Cromolyn Sodium (Intal) vs traditional Cromolyn Sodium nebulization in preventing airway inflammation in a high risk group of intubated premature neonates.

**Technical Approach:** The study population will consist of premature infants born at 32 weeks gestation and less, who are placed on mechanical ventilation. Those infants for which informed parental consent has been obtained will be randomized to receive either 3 mg Cromolyn via direct intra-tracheal instillation every 6 hours for 16 doses or 20 mg by nebulization every 6 hours for 16 doses. The doses will be started within 12 hours of being placed on a ventilator. At 48, 72, and 96 hours after the first dose is given, the infant will undergo tracheobronchiolar lavage. The lavage fluid will be analyzed for number and type of inflammatory cells as well as for the presence of chemical mediators of inflammation. Analysis of data will be by CHI-square and Student's t-test. Variables that will be considered in the analysis will be use of antenatal steroids, surfactants, antibiotics, indomethacin, diuretics and bronchodilators.

**Progress :** 12 subjects entered during study period. There is not enough complete data to analyze at this time. There are several reasons enrollment in this protocol has been slow with the two major reasons being that there was competition for patients with a nursing surfactant protocol which has since been completed and the PI was on TDY for over 3 1/2 months.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/025	<b>Status:</b> On-going
<b>Title:</b> Fetal Development[colon] Are Undiagnosed Maternal Inborn Errors of Metabolism Associated With Poor Intrauterine Growth and Congenital Malformations in the Developing Fetus		
<b>Start Date:</b> 12/17/93	<b>Est. Completion Date:</b> May 95	
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Thomas D. Carver, MC		
<b>Associate Investigators:</b> James R. Wright, M.T. LTC Arthur S. Maslow, MC CPT Andrew J. Bauer, MC		
Katherine H. Moore, Ph.D. MAJ Jerome N. Kopelman, MC MAJ Katherine S. Foley, MC		
<b>Key Words:</b> metabolism, fetal development, malformations, fetal death		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objective:** To determine if previously undiagnosed maternal inborn errors of metabolism (amino acidemias or organic acidurias) are a significant cause of fetal growth retardation, fetal malformations and fetal demise.

**Technical Approach:** In this controlled prospective study, the serum amino acid and urine organic acid contents will be evaluated in 3 groups of pregnant women. Group 1 will consist of women who have had 2 or more spontaneous abortions, a stillbirth, or have delivered a child identified as growth retarded, microcephalic, mentally retarded or with congenital anomalies. Group 2 will be the control group and consist of women who have had no more than 1 spontaneous abortion, or have delivered children with no known anomalies or are pregnant for the first time. Group 3 will consist of women not previously enrolled who are found during the pregnancy to have a fetus which is growth retarded ( $\leq$  3rd percentile on two ultrasounds 3-4 weeks apart), is microcephalic ( $\leq$  3 percentile on 2 ultrasounds 3-4 weeks apart), or has congenital anomalies.

The study questionnaire will be filled out at the time of entrance into the study and will consist of information pertaining to maternal educational and health history.

All samples will be sent to clinical investigation for storage until they can be analyzed. The blood samples will be frozen at -70 C until analyzed for quantitative amino acid content. The urine sample will be analyzed by GD Mass Spectroscopy for organic acid content. If both are normal then no further investigation will be done. If both are abnormal compared to published standards, the appropriate diagnostic work-up will be done to further identify the abnormality. All samples will be collected after an 8-12 hour fast to avoid post-prandial fluctuations in amino-acid concentrations. The study participants will be notified of their individual results (if abnormal) as they become known.

**Progress :** 203 subjects entered out of 300 needed. It is anticipated that by Marc 1996 we will have enrolled 130 women into group 1, 80 into group 2, and 25 into group 3. It is felt at that time we will be able to stop patient enrollment and begin data analysis.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/179		<b>Status:</b> On-going
<b>Title:</b> GLAXO Open Label Program for Patients with AIDS				
<b>Start Date:</b> 08/18/95		<b>Est. Completion Date:</b> Indef.		
<b>Department:</b> Pediatrics		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Mary P. Fairchok, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> HIV, Lamivudine (3TC), Zidovudine				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//

**Study Objectives:** To make available the therapeutic anti-retroviral agent, 3TC (lamivudine), in combination with zidovudine to patients with progressive, symptomatic Human Immunodeficiency Virus (HIV) disease who are refractory to all other approved therapies and unable to participate in any 3TC controlled clinical trials.

**Technical Approach:** This open label program offers 3TC (lamivudine) for an expected 2 to 3 pediatric patients with advanced disease ( $CD4 < 300$ ) who have been refractory to AZT and DDT. 3TC is a cytosine nucleoside analogue with potent in-vitro inhibitory activity demonstrated against HIV-1. High doses of 3TC have been tolerated over extended durations in toxicology trials providing no evidence to preclude clinical administration. This drug has been extensively studied to date in clinical phase I/II studies involving both pediatric and adult patients demonstrating good tolerance at doses up to 20 mg/kg/day with minimal toxicity. This drug is now available on an open label basis for compassionate use in adult and pediatric patients. The 3TC open label program has been approved and reviewed by the Ethical Review Committee (Kansas). Background demographic data of all patients will be summarized and displayed. Baseline values on study related diagnoses and lab tests will be compared with results obtained during and at the end of the study period. Lab abnormalities will be summarized and displayed by toxicity grade and dose level. Dropout/withdrawal rates and incidences of adverse events and AIDS-defining illnesses will be summarized and displayed by treatment regimen.

**Progress :** At present, only 2 subjects have been screened.

### Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 90/092

**Status:** On-going

**Title:** Core Project[colon] Evaluation of Diagnostic Assays for Human Immunodeficiency Virus (HIV) in Children with Evidence of HIV Exposure or HIV Illnesses

**Start Date:** 07/20/90

**Est. Completion Date:** Sep 91

**Department:** Pediatrics

**Facility:** MAMC

**Principal Investigator:** MAJ Mary P. Fairchok, MC

**Associate Investigators:**  
MAJ Thomas A. Perkins, MC  
COL Marvin S. Krober, MC

COL James S. Rawlings, MC  
LTC Joanna C. Beachy, MC

**Key Words:** HIV,diagnostic assays,children

Accumulative	Est. Accumulative	Periodic Review:
MEDCASE Cost: \$0.00	OMA Cost: \$0.00	//

**Study Objective:** To analyze laboratory assays for detection of HIV infection in children and to correlate the results with the clinical status of the child.

**Technical Approach:** This will be a multicenter study funded by Walter Reed Army Medical Center. The plan of this protocol is to evaluate the usefulness of new assays as they are developed, using blood from HIV-infected or high risk children. Blood will be sent to the laboratory for standard HIV testing using those tests that are most developed. Surplus will be utilized for less well developed assays or stored for future analysis. Results from the tests will be compared to conventional assays used to diagnose adult HIV infection, such as ELISA, western blot, and culture, to determine their usefulness in children. These specimens will also be used to develop improvements and new methods for HIV testing in children. This analysis will be done in 120-150 individuals at three month intervals to determine if changes in these tests correlate with changes in the patient's clinical or immunological status. Most of the data generated in this protocol will be qualitative and will be correlated to quantitative clinical data using Spearman's Rank Correlation. Logistic regression will be used for correlating the numerical data to noncontinuous clinical measures. Analysis of data from different clinical groups (patients who remain asymptomatic versus those who develop AIDS) will be compared using two-way ANOVA to determine significant differences between clinical groups.

**Progress :** 3 subjects have been entered at MAMC

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/085		<b>Status:</b> On-going	
<b>Title:</b> Parental Assessment of Psychologic Adjustment in Children with Asthma[colon] A Comparison of the Child Behavior Checklist and the Behavior Assessment System for Children					
<b>Start Date:</b> 03/17/95			<b>Est. Completion Date:</b> Jul 95		
<b>Department:</b> Pediatrics			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Patrick C. Kelly, MC					
<b>Associate Investigators:</b> MAJ Robert A. Byrne, MC			LTC Patrick C. Kelly, MC S.E. Greefkens		
<b>Key Words:</b> Asthma:psychologic adjustment, Child Behavior Checklist, Behavior Assessment System for Children					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> //

**Study Objective:** 1) To assess the correlation between the Child Behavior Checklist (parent report) and the Behavior Assessment System for Children (parent report) in assessing the social and emotional statuts of a group of children and adolescents with asthma. 2) To assess the impact of disease severtiy on the social and emotional status of this population. 3) To assess the impact of moves or service member deployment on the social and emotional status of this population.

**Technical Approach:** Sixty subjects, ages from 8 to 16 years and including approximately equal number of males and females, who have chronic asthma will be identified through review of Pediatric Pulmonary Clinic files and review of upcoming appointments. After consent has been obtained the mother of these subjects will be asked to fill out both the CBCL and the Parent Report Form of the BASC. In addition, a brief questionnaire inquiring about the subjects health status, recent moves, and service member deployments will be completed by the mother. When data collection is complete, it will be analyzed as follows. Correlation between the various scales of the CBCL and BASC will be analyzed using paired T tests. ANOVA will be used to study the relationship between disease severity and several scales on the CBCL. An unpaired T test will be used to study the relationship between recent moves or parent deployment and several scales on the CBCL.

**Progress :** 30 subjects have been entered, data analysis still pending.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/137		<b>Status:</b> Completed	
<b>Title:</b> A Phase III Multiple Dose Use Study of APAP Extended Release Pediatric Suspension Compared to Children's Tylenol Elixir in the Treatment of Febrile Children					
<b>Start Date:</b> 08/05/94			<b>Est. Completion Date:</b>		
<b>Department:</b> Pediatrics			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL Marvin S. Krober, MC					
<b>Associate Investigators:</b> CPT Kevin M. Creamer, MC			C. Jung CPT Katherine M. Hermann, MC		
<b>Key Words:</b> fever, APAP, Tylenol					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> //

**Study Objective:** To compare the antipyretic effect, side effects, and overall product acceptability of acetaminophen extended release pediatric suspension (320 mg/5 ml) compared to acetaminophen elixir 160 mg/5 ml, in the treatment of febrile children at home in a multiple dose use study.

**Technical Approach:** Patients entering this study will have two consecutive temperatures taken at least 15 minutes apart. The baseline temperature must be  $\geq 102.0^{\circ}\text{F}$  to  $105.5^{\circ}\text{F}$  rectally or  $\geq 101.0^{\circ}\text{F}$  to  $104.5^{\circ}\text{F}$  orally. Patients will then receive acetaminophen elixir 10-15 mg/kg or acetaminophen extended release pediatric suspension at 20-30 mg/kg. The Extended Release treated group will have temperatures taken at 0, 1, 2, 4, 6, 8, and 10 hours after the initial dose. After the initial dose, subsequent identical doses should be given every 8 hours thereafter as needed for temperature of  $>101.0^{\circ}\text{F}$  up to a maximum of 3 doses/day. The Elixir treated group will have their temperature taken at the same interval and subsequent doses should be given every 4 hours thereafter for temperatures of  $> 101.0^{\circ}\text{F}$  up to a total daily maximum of 5 doses. Daily telephone follow-up will be performed by the nurse and a follow-up evaluation will be made in the clinic on day 4.

**Progress :** A total of 19 patients were randomized. There was one serious adverse event. Data analysis is pending.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/160		<b>Status:</b> Completed	
<b>Title:</b> Variation in Pregnancy Outcomes Among Active Duty Junior Enlisted Women in Relation to W.I.C. Program Participation					
<b>Start Date:</b> 06/16/95			<b>Est. Completion Date:</b> Jan 95		
<b>Department:</b> Pediatrics			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL James S. Rawlings, MC					
<b>Associate Investigators:</b>			Virginia B. Rawlings, R.D.		
<b>Key Words:</b> WIC Program, Army enlisted women, pregnancy					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//	

**Study Objectives:** To measure differences in various pregnancy outcomes, among active duty junior enlisted (E1-E4) women who deliver at MAMC, between Women, Infants, and Children (W.I.C.) Program participants and non-W.I.C. women.

**Technical Approach:** Prospectively compiled data, pertaining to all deliveries of active duty E1-4 women at MAC from 1 January 1990 through 31 December 1994 will be analyzed for pregnancy outcomes in relation to W.I.C. Program participation. Approximately 1,300 women between 18 and 24 years of age are expected to be reviewed. Outcome parameters to be compared will be birth weight, gestational age, birth weight in relation to gestational age, perinatal mortality, and duration of neonatal hospital stay. Maternal risk factors for poor pregnancy outcome and demographic variables will be considered in the analysis. Cohort comparisons by chi-square analysis or Fischer's exact test of discontinuous data, and Student's T test of continuous data.

**Progress :** 1326 subjects delivery data was reviewed. Manuscript is being written.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/121		<b>Status:</b> On-going	
<b>Title:</b> Effectiveness of Spontaneous Labor at Term in Relation to the Hour of Onset					
<b>Start Date:</b> 03/17/95			<b>Est. Completion Date:</b> Mar 95		
<b>Department:</b> Pediatrics			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL James S. Rawlings, MC					
<b>Associate Investigators:</b>			COL John A. Read II, MC		
<b>Key Words:</b> Labor:spontaneous, labor:hour of onset					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//	

**Study Objective:** To measure the duration of labor, need for pharmacological augmentation and clinical outcomes of spontaneous labors at term in relation to the hours of onset and hour of delivery.

**Technical Approach:** Data will be prospectively compiled from all deliveries at MAMC following spontaneous onsets of labor at term (>36 weeks of gestation) during the period of 1 January 1985 through 31 December 1994. The records will be analyzed for duration of labor, need for pharmacological augmentation of labor, and neonatal outcomes in relation to hours of onset of labor and hour of delivery. Neonatal outcome parameters to be compared will be fetal distress, Apgar scores, perinatal mortality, and duration of neonatal hospital stay. Maternal risk factors for poor pregnancy outcome and demographic variables will be considered in the analysis. Data will be analyzed using chi-square analysis or Fischer's Exact Test of discontinuous data, and analysis of variance or the Student's T Test of continuous data.

**Progress :** 4931 subjects have been entered. Short interpregnancy intervals were more frequent among black than among white women. A total of 7.7 percent of the black women and 3.2 percent of the white women delivered premature, low-birth-weight infants ( $p < 0.001$ ). Among the black women, an interpregnancy interval of less than nine months was associated with significantly greater prevalence of preterm delivery and low birth weight in the neonates. Among the white women, only intervals of less than three months between pregnancies were associated with a greater prevalence of prematurity and low birth weight in infants.



**DETAIL SHEETS FOR PROTOCOLS**

**PHYSICAL MEDICINE & REHABILITATION SERVICE**

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/157		<b>Status:</b> On-going	
<b>Title:</b> The Effect of Pregnancy on the Performance, Health, and Nutritional Status of Postpartum Soldiers					
<b>Start Date:</b> 09/21/94			<b>Est. Completion Date:</b> Sep 95		
<b>Department:</b> Physicial Medicine & Rehabilitation Service			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Joseph R. Dettori, MC					
<b>Associate Investigators:</b> LTC Kathleen A. Westphal, MC CPT Anthony Pusateri, MS			COL Paul N. Smith, MC LTC Alana D. Cline, MS T.M. Vanderline		
<b>Key Words:</b> female soldiers:pregnancy, health					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		//

**Study Objective:** (1) To determine the proportion of soldiers who return to their preconception fitness level at their first postpartum APFT, and to compare; (2) distribution, incidence and risk of injury and illness between postpartum soldiers and nonpregnant, non-postpartum soldiers; (3) changes in weight and body composition between soldiers and family members in the postpartum period; (4) bone mineral status between late pregnant and postpartum soldiers and their family members; (5) nutritional status between late pregnant and postpartum soldiers and family members; (6) iron and folate status among late pregnant and postpartum soldiers, late pregnant and postpartum family members, and nonpregnant, non-postpartum soldiers.

**Technical Approach:** Women in their third trimester of pregnancy will be identified through the OB-GYN clinics at their respective hospitals and asked to volunteer for the study. Non-pregnant soldiers will be solicited through the unit chain of command.

Full-time health personnel hired for the study at each site will measure the dependent variables and collect the data. Study health personnel will be supervised by an Army obstetrician. Study subjects will undergo blood draws to assess iron, folate and calcium status; anthropometric measurements to determine body composition, dual energy x-ray absorptiometry to measure bone mineral density and to validate body fat evaluations. Fitness will be assessed using the last pre-pregnancy Army Physical Fitness Test scores and the first postpartum APFT scores for all soldiers in the study. Medical records of all soldiers will be reviewed monthly to record all injuries and illnesses. Demographics, health habits and diet history, and exercise before, during and following pregnancy will be obtained through questionnaires.

**Progress :** 120 pregnant soldiers, 115 pregnant family members and 60 non-pregnant soldiers are enrolled in this study. Initial measurements of bone mineral density and body composition along with detailed nutritional and activity data have been obtained. Twelve subjects have completed their six-month follow-up measurements and medical records review.

**DETAIL SHEETS FOR PROTOCOLS**

**PREVENTIVE MEDICINE SERVICE**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/090		<b>Status:</b> On-going	
<b>Title:</b> Clinical Trial to Compare Two Smokeless Tobacco Cessation Programs					
<b>Start Date:</b> 04/01/94			<b>Est. Completion Date:</b> Jul 95		
<b>Department:</b> Preventive Medicine			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Kathie J. Brendemuhl, RN					
<b>Associate Investigators:</b> S.S. VanBeuge			MAJ Jeffrey D. Gunzenhauser, MC		
<b>Key Words:</b> smoking cessation:smokeless tobacco					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//	

**Study Objective:** The objective is to ascertain whether either of two treatment regimens is more effective in assisting individuals in cessation from use of smokeless tobacco products.

**Technical Approach:** This is a clinical trial which will compare the effectiveness of two regimens on smokeless tobacco cessation rates. Users of smokeless tobacco products in the Fort Lewis and McChord Air Force Base communities will be recruited to participate in a tobacco cessation program designed specifically for smokeless tobacco users. Potential volunteers will be screened through the use of a questionnaire and a limited history and physical examination. After obtaining informed consent, participants will be randomized to receive one of two treatment regimens. Both treatment groups will receive physician advice to quit using tobacco products and will be prescribed nicotine replacement therapy in accordance with the Madigan Army Medical Center (MAMC) prescribing protocol. In addition, the first treatment group (phone counseling) will receive an initial face-to-face counseling session with the study nurse during which time a quit date will be selected, standardized written materials will be provided, and follow-up procedures will be reviewed; subsequently each participant in this treatment group will receive four (4) phone follow-up consultations at 48 hours, 1 week, 3 weeks, and 6 weeks after the preselected quit date. The second treatment group (Freshbreath) will participate in the FRESHBREATH smokeless tobacco behavior change therapy course, a 6-hour course, meeting as a group twice a week (1.5 hours each session) for two weeks. During the course of the trial (1 year), participants in both groups will have access to the study nurse or physician to address specific needs or problems. Cessation rates will be monitored by self-report during phone interviews at 3 months, 6 months, and 1 year. Differences in cessation rates will be assessed through multivariate analysis. Determinants (confounders) of cessation other than treatment group will be included in the analytic model. Statistically significant results will be interpreted at the 0.05 level of significance.

**Progress :** Funding continues to be sought.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/079	<b>Status:</b> On-going
<b>Title:</b> Soldier HIV Behavior Modification		
<b>Start Date:</b> 02/17/95	<b>Est. Completion Date:</b> Sep 96	
<b>Department:</b> Preventive Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Roberta E. Dyer		
<b>Associate Investigators:</b> Debra Pontius		Ann E. Hyder
<b>Key Words:</b> HIV, behavior		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** 1. What is the current knowledge level concerning HIV and AIDS within the units, and does knowledge level change after the intervention? 2. What are the current beliefs toward HIV and AIDS, and risk behaviors regarding sexual practices, within the units and do beliefs and risk behaviors change after the intervention? 3. At the unit level is a peer led HIV education program more effective than the current nurse led HIV education program at increasing adaptive intentions and attitudes toward safe sex practices? These aims will be addressed utilizing the Health Belief Model as the theoretical framework.

**Technical Approach:** The purpose of this study is to determine if the use of a peer leader as opposed to the HIV nurse or the size of the group receiving the intervention makes any change in the outcome measures of knowledge of HIV and AIDS, beliefs toward HIV and AIDS, and risk behaviors. The theoretical model for this proposal is the Health Belief Model. The design of the study will include four groups receiving the intervention and a control group. The units requesting HIV education classes will be assigned to either a large or small group depending on the size of the unit and will receive the intervention from either the peer leader or the HIV nurse. This study will involve approximately 35 units with approximately 1700 soldiers. The units will be further stratified by their mission to allow for differences based on individual requirements to meet the unit mission. The control group will consist of units that do not request HIV education classes during the intervention period. The research questions will be analyzed using analysis of variance upon the data gathered from three questionnaires, and post hoc tests will be performed on significant differences. The first questionnaire will be administered prior to the intervention and will consist of a comprehensive assessment of knowledge, beliefs and risk behaviors. The second questionnaire will be administered immediately after the intervention and will focus on knowledge. The third questionnaire will be administered after three months and will focus on beliefs and risk behavior.

**Progress :** In process of hiring administrative and clinical personnel.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 90/014	<b>Status:</b> Completed
<b>Title:</b> Assessment of Risk Factors for HIV Infection Among Active Duty U.S. Army Personnel with Documented Recent HIV-Antibody Seroconversion - Incident Cases		
<b>Start Date:</b> 01/19/90	<b>Est. Completion Date:</b> Jun 91	
<b>Department:</b> Preventive Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Jeffrey D. Gunzenhauser, MC		
<b>Associate Investigators:</b> COL Kevin M. McNeill, MC                      MAJ John G. McNeil, MC MAJ Margot R. Krauss, MC		
<b>Key Words:</b> HIV,risk factors,antibody seroconversion		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 02/07/92

**Study Objective:** To assess demographic and behavioral determinants associated with new HIV infections in order to generate information for implementing changes in education strategies currently in use for populations at risk for HIV infection, particularly in terms of potential new risk factors.

**Technical Approach:** This multicenter study will be conducted using a case-control design. A case will be defined on the basis of seroconversion of antibody to HIV using ELISA with duplicate Western Blot confirmation. There will be one control for each male subject and three controls for each female subject. Controls will be selected at random from the group of all uninfected active duty personnel at the same installation where cases seroconvert and will be matched for age ( $\pm 2$  years), gender, ethnicity, rank, and length of service. Controls must have tested negative on or after the date their matched case seroconverted. Subjects and controls will be interviewed by trained interviewers from collaborating civilian health agencies who are blinded to the HIV antibody status of study participants. The interview will be conducted from and HIV Seroconversion Risk Factor Study form which is divided into the following sections: demographics, medical history, risk factors of drug use, sexual history, and other risks. The investigators anticipate that 160 to 230 incident cases will be eligible for recruitment each year and feel that the majority of these cases can be recruited. In any multi-risk factor study such as this, the problem of chance statistical considerations being made between exposure and outcome exists if repeated statistical testing is performed. For this reason, methods of analysis beyond statistical will be performed. These methods will include calculation of measures of effect (e.g. matched odds ratios and confidence intervals) for various risk behaviors as well as matched multivariate analyses (e.g. behavioral hazards, conditional logistic regression).

**Progress :** Protocol was completed by WRAMC. No subjects were entered from MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/011		<b>Status:</b> On-going	
<b>Title:</b> Comparative Morbidity Study of Active Duty Women Serving in Korea and Ft Lewis by MAJ Jeffrey D. Gunzenhauser, MC					
<b>Start Date:</b> 11/04/94			<b>Est. Completion Date:</b> Mar 96		
<b>Department:</b> Preventive Medicine			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Jeffrey D. Gunzenhauser, MC					
<b>Associate Investigators:</b>			J.A. Pavlin		
<b>Key Words:</b> Female soldiers, morbidity, Korea, Ft Lewis					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b>
					//

**Study Objective:** To describe the out-patient and in-patient morbidity experience of women serving in Korea and compare this to women serving at Ft. Lewis and to men at both locations and to describe behavioral risk factors of women serving in Korea.

**Technical Approach:** This is an epidemiologic study. Out-patient clinical events which are assessed at military clinics will be categorized into one of 14 specific morbidity categories: orthopedic/injury, respiratory, medical illness, dermatologic, bites/stings, environmental injury, diarrhea/GI, unexplained fever, sexually transmitted disease, ophthalmic, mental health, dental, substance abuse and miscellaneous. Diagnosis will be based on medical record entries (not chief complaints) and will be broken down by gender. Rates of health care usage for men will be estimated by counting all visits registered in clinic logs. One male record will be pulled for each female record pulled (the second male to visit the clinic after the index female visit).

In-patient morbidity experience of women will be studied by analyzing data from the Individual Patient Data System maintained at Ft. Sam Houston, TX. All hospitalization of men and women will be included in the analysis. Each hospitalization at the 121 General Hospital and at Madigan AMC will be classified into one of the 14 morbidity categories to allow broader comparisons with out-patient morbidity data and between genders and locations.

Health surveys will be mailed to a probability sample of female soldiers serving in Korea and at Ft. Lewis. Approximately 1000 women in Korea and 1000 women at Ft. Lewis will be targeted for this survey.

**Progress :** 4000 surveys were mailed. The response rate was approx. 65%. Data are currently being entered.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/031		<b>Status:</b> Completed	
<b>Title:</b> A Descriptive Analysis of Civilian Time-Loss Work-Related Injuries at Ft Lewis, 1989-1994					
<b>Start Date:</b> 01/20/95			<b>Est. Completion Date:</b> Jun 95		
<b>Department:</b> Preventive Medicine			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> D. C. Hack					
<b>Associate Investigators:</b>			MAJ Margot R. Krauss, MC		
<b>Key Words:</b> Injuries:work-related, time loss					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		//	

**Study Objectives:** To analyze the loss of time due to work-related injuries at Ft. Lewis from 1989 to 1994. To compare the time loss profile of the three largest categories of injuries at Ft. Lewis with a reference expected outcome profile. To compare the outcome profiles of employees treated by health care providers with training in Occupational Medicine with employees treated by providers without such training.

**Technical Approach:** An evaluation will be performed of all cases of civilian employees who have suffered work-related injuries resulting in time lost from work during the 1989-1994 period. Workers at Ft. Lewis are identified at the Department of Labor and Industries by a set of 4 digit CMD codes which are reserved for specific activities on Ft. Lewis and are applied to each case. Employee/patient privacy will be maintained because there will be no need to actually contact the employees/patients during the study. All the necessary information will be obtained from the records filed with the Department of Labor and with the Civilian Personnel Office at Ft. Lewis. The only exception is that it may be necessary to contact the applicable health care providers to ascertain their level of training in Occupational Medicine. A lost-time injury profile will be generated for Ft. Lewis showing the (1)type and extent of injuries, (2) resultant loss of work time, (3) medical treatment costs, (4) health care provider type, (5) return to light duty time, and (6) return to full duty time. The information for the three major categories of injuries will then be compared with standard profile for comparable injuries. In addition, the types of health care providers will be compared to evaluate for differences in return to light and/or full duty.

**Progress :** There were 340 workers who received injuries resulting in two or more days off work during the study period. More than 85% of these workers returned to work within the first thirty days. Health care providers were a mix of employer-provided Occupational Medicine providers, employee-selected providers with training in Occupational Medicine, and employee-selected providers without such training.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/054	<b>Status:</b> Completed
<b>Title:</b> Inpatient Morbidity Patterns in Active Duty Army Females at Fort Lewis from 1989-1993		
<b>Start Date:</b> 01/20/95	<b>Est. Completion Date:</b> Jun 95	
<b>Department:</b> Preventive Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Rose Marie Hendrix, MC		
<b>Associate Investigators:</b> MAJ Jeffrey D. Gunzenhauser, MC		MAJ Margot R. Krauss, MC
<b>Key Words:</b> Morbidity, Army active duty females		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

Study Objective: 1) To describe the inpatient morbidity experience of active duty army females at Fort Lewis. 2) To compare the female morbidity to that of active duty army males at Fort Lewis.

Technical Approach: Data from the Individual Patient Data System (IPDS) for all active duty Army admissions to Madigan Army Medical Center from 1 Jan 1989 to 31 Dec 1993 will be described and analyzed. Diagnosis codes will be grouped by system, and by disease/injury categories, and specific morbidity rates calculated using Fort Lewis active duty population as the denominator. Repeat admission for the same diagnosis will be eliminated from the analysis of rates. Rates will be compared between males and females and rate ratios calculated. Identification of conditions which are most frequently responsible for the hospitalization of Army women, and of conditions for which Army women have higher admission rates than Army men will allow the targeting of future research and public health interventions toward these conditions.

Progress : 16,000 records were reviewed, data analysis is almost complete.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/032	<b>Status:</b> Completed
<b>Title:</b> Vaccine Usage in Soldiers at Fort Lewis, WA[colon] Enumeration of Unnecessary Vaccinations		
<b>Start Date:</b> 01/20/95	<b>Est. Completion Date:</b> Jun 95	
<b>Department:</b> Preventive Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> S.D. Klamerus		
<b>Associate Investigators:</b> MAJ Margot R. Krauss, MC		
<b>Key Words:</b> vaccinations, soldiers		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objectives:** To determine whether a significant number of vaccines are given inappropriately to soldiers at Fort Lewis and at Madigan Army Medical Center. Also, to characterize inappropriate vaccine administration by type of vaccine and setting of administration.

**Technical Approach:** This study will utilize a random terminal digit, sampling 4% of all soldiers registered in the Ft. Lewis personnel database (SIDPERS) as of 1 Oct 1994 (approximate sample size of 500). For each of the subjects, a complete vaccination history will be obtained from medical records, yellow shot records and, where available, unit readiness databases. A self-administered questionnaire will be mailed to each subject to determine assignment and deployment history for the prior two years, and to report any vaccinations not in the records. Objective criteria for vaccination appropriateness, developed from manufacturers recommendations, Army policies and the Advisory committee on Immunization Practices guidelines are listed in Appendix B. All vaccination given to each subject during the year prior to the date of record review will be categorized as appropriate or inappropriate, given prior vaccination history and subsequent deployments. The overall rate of inappropriate vaccine administration for each type of vaccination, each general group of soldier type (combat arms, support or service support), and possibly, each type of administrative site (immunization clinic, TMC, aid station, or Soldier Readiness Program Site) will be calculated with confidence intervals.

**Progress :** Of 605 document immunization doses, 29.4% were determined to be inappropriate. Meningococcal, MMR, tetanus, and Japanese encephalitis immunizations had the highest rates of inappropriate administration. Soldiers assigned to Fort Lewis less than one year and soldiers who had participated in less than three readiness exercises had lower rates of inappropriate administration.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 93/009	<b>Status:</b> On-going
<b>Title:</b> Low-Dose Oral Contraceptives and Cardiovascular Disease		
<b>Start Date:</b> 10/02/92	<b>Est. Completion Date:</b>	
<b>Department:</b> Preventive Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Margot R. Krauss, MC		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> oral contraceptives, cardiovascular disease		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objective:** To assess demographic and behavioral determinants associated with new HIV infections in order to generate information for implementing changes in education strategies currently in use for populations at risk for HIV infection, particularly in terms of potential new risk factors.

**Technical Approach:** This multicenter study will be conducted using a case-control design. A case will be defined on the basis of seroconversion of antibody to HIV using ELISA with duplicate Western Blot confirmation. There will be one control for each male subject and three controls for each female subject. Controls will be selected at random from the group of all uninfected active duty personnel at the same installation where cases seroconvert and will be matched for age ( $\pm 2$  years), gender, ethnicity, rank, and length of service. Controls must have tested negative on or after the date their matched case seroconverted. Subjects and controls will be interviewed by trained interviewers from collaborating civilian health agencies who are blinded to the HIV antibody status of study participants. The interview will be conducted from and HIV Seroconversion Risk Factor Study form which is divided into the following sections: demographics, medical history, risk factors of drug use, sexual history, and other risks. The investigators anticipate that 160 to 230 incident cases will be eligible for recruitment each year and feel that the majority of these cases can be recruited. In any multi-risk factor study such as this, the problem of chance statistical considerations being made between exposure and outcome exists if repeated statistical testing is performed. For this reason, methods of analysis beyond statistical will be performed. These methods will include calculation of measures of effect (e.g. matched odds ratios and confidence intervals) for various risk behaviors as well as matched multivariate analyses (e.g. behavioral hazards, conditional logistic regression).

**Progress :** 5 subjects were entered at MAMC, enrollment continues.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/158		<b>Status:</b> Completed	
<b>Title:</b> Risk Factors for Lead Poisoning in Children of Ft Lewis Personnel					
<b>Start Date:</b> 09/02/94			<b>Est. Completion Date:</b> Apr 94		
<b>Department:</b> Preventive Medicine			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Ann A. Yackovich, MC					
<b>Associate Investigators:</b>			MAJ Margot R. Krauss, MC		
<b>Key Words:</b> lead poisoning, children, Ft Lewis					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//	

**Study Objective:** To assess the risk factors for lead poisoning in children of Ft. Lewis active duty personnel.

**Technical Approach:** A self-administered questionnaire will be mailed to a sample of Ft. Lewis personnel with children under six years of age. The survey will include questions on housing (peeling paint, age, location), use of various ethnic remedies (which will be specifically named in the survey question so that there is no confusion on the part of the respondent), and any hobbies or occupations of the adult members of the household which could increase the children's exposure to lead. The hobbies/occupations question will be in two parts: part will include a listing of specific hobbies and occupations and the other part will be short answer, allowing the respondent to add any pertinent information or suggest something that is not specifically listed.

The survey will also include several additional questions on other childhood risk factors such as use of bicycle helmets, childproofing in the home, and use of car safety seats. Analysis of variance and logistic regression will be performed; variables will include race, sex, location of housing, use of ethnic remedies, hobbies, and occupation.

**Progress :** 1000 subjects entered, data analysis is almost complete.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF RADIOLOGY**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/119		<b>Status:</b> On-going	
<b>Title:</b> Gallbladder Ejection Fractions					
<b>Start Date:</b> 06/09/93			<b>Est. Completion Date:</b> Dec 94		
<b>Department:</b> Radiology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC John M. Bauman, MC					
<b>Associate Investigators:</b>			Jerome Billingsley, M.D.?		
MAJ Michael F. Lyons II, MC			LTC Clifford L. Simmang, MC		
MAJ Richard R. Gomez, MC					
<b>Key Words:</b> gallbladder, ejection fractions					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$6166.00		//	

**Study Objective:** To determine the clinical usefulness and reproducibility of gallbladder ejection fractions.

**Technical Approach:** Fifty volunteers will be studied on two occasions utilizing half of the normal radiopharmaceutical dose. These studies will be separated by no more than 30 days. Subjects will be given an injection of approximately 2.6 millicuries Tc-99m-DISIDA and serial one minute computer acquired images will be obtained for a maximum of 60 minutes. Once maximal gall bladder activity is achieved by visual inspection, 0.01 micrograms/kilogram sincalide will be given intravenously for three minutes via infusion pump. Serial one minute computer acquired images will be obtained for 30 minutes following this infusion. The results of the studies will not be used to determine patient care. The patient will be scheduled for cholecystectomy after the second DISIDA scan is completed. The gallbladder will be submitted to pathology for pathologic evaluation. The patient will complete a questionnaire prior to, and at one and six months post cholecystectomy. Mean, range, and standard deviation for each set of data will be calculated. A repeated measures ANOVA will be calculated.

**Progress :** 11 patients have been enrolled. Protocol remains open to patient accrual.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/077		<b>Status:</b> On-going	
<b>Title:</b> Determination of Normal Regional Myocardial Thallium Distribution and Development of a New Display Technique					
<b>Start Date:</b> 05/06/94			<b>Est. Completion Date:</b> Jul 94		
<b>Department:</b> Radiology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC John M. Bauman, MC					
<b>Associate Investigators:</b> Jerome Billingsley, M.D.?			COL Stanton R. Brown, MC James H. Timmons, MD		
<b>Key Words:</b> thallium, myocardial distaribution, new technique					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//	

**Study Objective:** (1) To determine the normal regional variation in the myocardial distribution of <sup>201</sup>Tl. (2) To use this information to create a color translation table for semiquantitative analysis of Thallium images. (3) To evaluate the ability of the new translation table to predict the presence or absence of significant coronary artery lesions at cardiac catheterization.

**Technical Approach:** We intend to pull all Thallium studies and cardiac catheterization data on patients who have had both studies at MAMC since 1 August, 1992. Results of Thallium and catheterization studies will be entered on worksheets and from there into a computerized database.

We will review a minimum of 10 data sets where both the Thallium study and catheterization data are normal. The relative distribution of Thallium on the stress studies will be quantitated using a circumferential image profile on the short axis slices using 8 mid-ventricular slices which demonstrate a complete left ventricular chamber.

Sixty values will be calculated for each of eight central stress slices. The maximum and minimum count values for all slices will give us the range of normal Thallium variation for each patient's stress study. This value, will be expressed as a percent of the maximum uptake. Finally the mean, range and standard deviation for the 10 patients' percent normal variations will be calculated.

The color map will be created using the information from phase I. All images are limited to a maximum of 256 gray levels. We will divide these 156 levels into only 5 colors for our map. As a result, individual pixels will be colored according to their relative count value with respect to the maximum in the image. Break points for color levels will be determined by the mean percent normal variation and standard deviation.

The new color translation will then be used to reinterpret a minimum of 50 Thallium studies for which cardiac catheterization data is available. Studies will be read separately by 2 board certified nuclear medicine physicians without knowledge of the clinical history, previous Thallium result, exercise data or catheterization result. Using only the new color table, results will be annotated as normal or abnormal. If abnormal, location and extent of abnormality will be recorded. Actual colors of defects will be recorded and subsequent data analysis for correlation with the bull's eye plots, prior image interpretations and cardiac cath data will be made for each color level of defect.

**Progress :** Basic data has been collected. Need to perform blinded review of studies to evaluate the color table, then look prospectively. 50 catheterization correlations have been performed and are ready for review.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/028		<b>Status:</b> Terminated	
<b>Title:</b> Quantitative Pulmonary Perfusion					
<b>Start Date:</b> 12/04/92			<b>Est. Completion Date:</b> Jan 93		
<b>Department:</b> Radiology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC John M. Bauman, MC					
<b>Associate Investigators:</b>			MAJ Stephen E. Budd, MC		
<b>Key Words:</b> pulmonary perfusion					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$1490.00	//	

Study Objective: To determine the normal split lung function and reproducibility of quantitative lung perfusion with technetium macro aggregated albumin (99mTc-MAA).

Technical Approach: All volunteers will receive pulmonary spirometry and a chest x-ray to determine normalcy of volunteers. All female volunteers and in child bearing age will have a negative serum beta-HcG documented. While in the supine position an IV injection of approximately 1.5 millicuries 99mTc-MAA (less than half the usual dose given at MAMC for diagnostic pulmonary studies) will be administered. Both anterior and posterior images of 800,000 counts will be computer acquired and a geometric mean will be calculated and reported. A second study utilizing the same dose will be done within 2 weeks of the initial study, but will not require repeat spirometry or chest x-ray.

Progress : No patients were enrolled in FY95. Protocol was terminated due to poor patient accrual.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/038		<b>Status:</b> On-going	
<b>Title:</b> Digitally Acquired Radiographic Air Contrast Barium Enema vs. Colonoscopy in Polyp Detection, Cancer Detection, and cost in a Federal Tertiary Care Center					
<b>Start Date:</b> 12/17/93			<b>Est. Completion Date:</b> Jan 95		
<b>Department:</b> Radiology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Gregory N. Bender, MC					
<b>Associate Investigators:</b> MAJ Michael F. Lyons II, MC			MAJ Amy M. Tsuchida, MC CPT Thomas P. Peller, MC		
<b>Key Words:</b> polyps, barium enema, colonoscopy					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		//	

Study Objective: To determine if digitally acquired radiographic air contrast barium enema (DAR-ACBE) examinations of the colon might serve as a cost effective surrogate to colonoscopy in the MAMC colon cancer screening program.

Technical Approach: By obtaining DAR-ACBE and colonoscopy on the same patient a test of diagnostic equality for these two examinations will be performed. The diagnostic equality of these examinations will be tested by assessing their ability to find polyps >5mm in size and in finding cancers of any size.

Progress : Enrollment of patients has been delayed due to funding.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/166		<b>Status:</b> On-going	
<b>Title:</b> Cost Effectiveness of Early Technetium 99m Bone Scintigraphy in Traumatic Wrist Injury					
<b>Start Date:</b> 08/18/95			<b>Est. Completion Date:</b> Feb 96		
<b>Department:</b> Radiology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT John D. Crocker, MC					
<b>Associate Investigators:</b> LTC John M. Bauman, MC			Rush A. Youngberg		
<b>Key Words:</b> Wrist, scintigraphy, cost effectiveness					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//	

**Study Objective:** To determine the cost effectiveness and utility of scintigraphy in the management of patients with traumatic wrist injury whose initial radiographs are negative, yet who clinically are felt to have scaphoid fractures.

**Technical Approach:** This is a prospective blinded study to determine the cost effectiveness of a more accurate, slightly more expensive imaging modality in the management of patients with traumatic wrist injury. All patients over 18 years of age with a fall on the outstretched hand (a "FOOSH" injury) will be included. One hundred patients will be enrolled.

Those enrolled in the study will undergo a limited high resolution bone scan of each wrist (the uninjured wrist will serve as a comparison to the injured wrist) within 48-96 hours of the time of injury. When the clinician has determined that management is complete, the clinician will have access to the bone scan results, prior to the patients' discharge from care.

The radiographs will be reviewed by the chief of musculoskeletal radiology, the bone scans by a staff nuclear medicine physician, and the clinical evaluation and follow-up will be performed per usual orthopedic clinic practice at MAMC. Costs will be calculated based on the CHAMPUS allowable reimbursement for the services rendered as defined by the 1995 CPT codes of the American Medical Association. Data analysis will include determining if there is statistical significance between the costs of caring for clinically "false positive" fractures and the costs of early bone scintigraphy.

**Progress :** Protocol has just begun, only 1 subject entered. Further work on capturing patients for the study is on-going.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/030		<b>Status:</b> Completed	
<b>Title:</b> Decompression of Acute Colonic Pseudo-obstruction With A Tricomponent Coaxial System Under Fluoroscopy					
<b>Start Date:</b> 02/04/94			<b>Est. Completion Date:</b> Dec 93		
<b>Department:</b> Radiology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Daniel D. Do-Dai, MC					
<b>Associate Investigators:</b>			LTC Gregory N. Bender, MC		
<b>Key Words:</b> colonic obstruction decompression, fluoroscopy					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//	

**Study Objective:** To respectively review all the colonic decompression of pseudo-obstruction with a tricomponent coaxial system (TAS) under fluoroscopy performed between 1 March 1992 and 1 August 1993 to determine the related morbidity and mortality. The study will also attempt to introduce methods or techniques that can prevent the risks of bleeding and colonic perforation.

**Technical Approach:** This study will retrospectively review the following information: indication, procedure time, indwelling decompression catheter time, complications of bleeding and colonic perforation and rate of recurrence of pseudo-obstruction after removal of decompression catheter.

**Progress :** No subjects entered in FY 95, 5 patients were entered in FY 94. Colonic decompression with TAS was successfully performed on all 5 patients without associated complications of bowel perforation or bleeding. Patient comfort was enhanced immediately after placement of the TAS. Complete decompression was observed in all patients within 6-48 hours. There was no recurrence after removal of the TAS.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/125		<b>Status:</b> Terminated	
<b>Title:</b> Cine MRI of the Temporomandibular Joint as an Adjunct to Standard Open and Closed Mouth Images					
<b>Star Date:</b> 03/17/95		<b>Est. Completion Date:</b> Mar 96			
<b>Department:</b> Radiology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Theodore A. Dorsay, MC					
<b>Associate Investigators:</b>			Rush A. Youngberg		
<b>Key Words:</b> Mouth:imaging, joint:temporomandibular, Cine MRI					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//	

**Study Objective:** To retrospectively describe and demonstrate the advantages of cine loop magnetic resonance imaging (MRI) in diagnosis of functional and anatomic temporomandibular joint (TMJ) disease as an adjunct to conventional open and closed mouth MRI views by qualitatively evaluating the Madigan Army Medical Center experience with this technique.

**Technical Approach:** Patients with high clinical suspicion of internal derangement of the TMJ have been evaluated both pre-and post-intervention with MRI as an adjunct to their work-up by the Department of Oral and Maxillofacial Surgery. A spectrum of internal derangements of the TMJ as well as post-interventional evaluation have been imaged. For the past year, closed loop cine has been a part of our evaluation in addition to the normal open and closed mouth standard sequences. The investigators will retrospectively review all MRI studies of the TMJ and decide if open and closed mouth still images alone were enough to make adequate diagnosis as compared to the closed cine loop. Cases where cine MRI changed or modified the diagnosis will be grouped to pathology and expounded on. Clinical histories will be evaluated to determine affect on treatment if any. Analysis will be qualitative, descriptive, and anecdotal. Pathologies not obvious or completely evaluated by open and closed mouth images alone will be discussed and demonstrated in video format.

**Progress :** No subjects were entered. Project terminated due to lack of time by PI.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/124		<b>Status:</b> On-going
<b>Title:</b> Measurement Accuracy of Reformatted MR Images in Cardiac Imaging Using A Pig Cadaveric Model				
<b>Start Date:</b> 06/09/93		<b>Est. Completion Date:</b> Jul 93		
<b>Department:</b> Radiology		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Vincent B. Ho, MC				
<b>Associate Investigators:</b>		SSG James Adams, NCOIC		
<b>Key Words:</b> MRI, cardiac imaging, pig model				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//

**Study Objective:** To determine the accuracy of reformatted images in the measurement of cardiac wall thickness.

**Technical Approach:** The cadaveric hearts of five pigs will be flushed, filled with and suspended in 10% formalin solution. Vitamin E capsules (visible on MRI) will be attached to the outside of the heart to mark the "long-axis" plane. MRI will then be performed in planes parallel to and oblique to the "long-axis". Reformatted images from obliquely acquired MRI images will be measured for ventricular wall thickness as determined from the "long-axis" view and compared with measurements obtained in the true "long-axis" view. The cadaveric pig hearts, once imaged, will be biplaned and true ventricular wall thicknesses will be measured. The cadaveric measurements will also be compared with those obtained by MRI.

The ventricular wall thickness as determined by (1) direct "long-axis" MR, (2) reformatted "long-axis" views, and (3) actual necropsy measurement of the cadaveric heart will be evaluated for degree of variance and statistical significance.

**Progress :** 4 pigs have been scanned awaiting MRI software upgrade to measure wall thickness.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95				<b>Protocol No.:</b> 95/037		<b>Status:</b> Completed	
<b>Title:</b> Ruptured Sinus of Valsalva Aneurysm[colon] Cine MR Charactyerization							
<b>Start Date:</b> 11/18/94				<b>Est. Completion Date:</b> Jan 95			
<b>Department:</b> Radiology				<b>Facility:</b> MAMC			
<b>Principal Investigator:</b> MAJ Vincent B. Ho, MC							
<b>Associate Investigators:</b>				J.B. Kinney			
<b>Key Words:</b> Aneurysm:valsalva, MR							
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>			
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$900.00		//			

**Study Objective:** The objective of this study is to describe the MRI (Magnetic Resonance Imaging) technique utilized in the characterization of the intracardiac fistulous communication of a patient with a ruptured sinus of Valsalva aneurysm.

**Technical Approach:** This study is a case report of the MRI strategy implemented in the evaluation of patient with a ruptured sinus of Valsalva aneurysm. Congenital sinus of Valsalva are relatively rare anomalies which are typically undetected unless they rupture. Ruptured aneurysms may present with heart failure or occasionally can be more indolent if the fistula formed is small. In our patient, the ruptured sinus of Valsalva presented as a new continuous low mid-precordial, grade 3/6 "to and fro" murmur. Utilizing cine MRI, the fistula between the non-coronary sinus of Valsalva and superior aspect of the right ventricle. Cine MRI is a relatively recent development which supplied crucial information for the identification of the fistulous communication in our patient. The delineation of the fistulous tract had serious pre-operative implications and aided in the surgical planning. This study is descriptive and illustrative.

**Progress :** Case analyzed and published in Journal of Computer Assisted Tomography, July/August 1995.

### Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 93/037

**Status:** On-going

**Title:** Arachnoid Granulations[colon] MR Features

**Start Date:** 02/05/93

**Est. Completion Date:** Feb 94

**Department:** Radiology

**Facility:** MAMC

**Principal Investigator:** MAJ Vincent B. Ho, MC

**Associate Investigators:**

MAJ Miquel J. Rovira, MC

**Key Words:** arachnoid granulations:MRI

**Accumulative**

**Est. Accumulative**

**Periodic Review:**

**MEDCASE Cost:** \$0.00

**OMA Cost:** \$0.00

//

**Study Objective:** The 600 MR studies performed since July 1992 will be reviewed for the presence of arachnoid granulations within the cerebral venous structures.

**Technical Approach:** All MR studies performed since July 1992 will be reviewed and evaluated for the presence of arachnoid granulations. The diagnosis of arachnoid granulation will be based on the conventional venographic descriptions (MRE angiography or traditional cerebral venography) as interpreted by radiologist. This is a study of description in which statistical analysis will not be necessitated.

**Progress :** 600 MRI reviewed. Pending cadaveric correlation from the Uniformed Services University of the Health Sciences.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/054		<b>Status:</b> On-going
<b>Title:</b> Urologic Stone Conspicuity[colon] Plain Films vs Computed Radiography				
<b>Start Date:</b> 03/05/93			<b>Est. Completion Date:</b> Apr 94	
<b>Department:</b> Radiology			<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Vincent B. Ho, MC				
<b>Associate Investigators:</b>			CPT Robert E. Vaughan, MC	
<b>Key Words:</b> urologic stones:conspicuity				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//

**Study Objective:** To compare conspicuity of urologic stones using conventional plain films vs. computed radiographs.

**Technical Approach:** Urologic stones sent for chemical/pathologic analysis will be radiographed by both conventional plain film and computed radiography. The stones will be radiographed with a "soft tissue" phantom to simulate normal human soft tissue density. The plain film/computed radiographs will then be independently interpreted for stone location and number by 5 - 10 radiologist/residents. The conspicuity of the stones on plain film will then be compared to that on the computed radiography acquired film. Blind films (i.e. films acquired without stones and only a soft tissue phantom) will be included to "blind" the readers.

Standard ROC curves among readers will be established and Student's t test analysis for statistical variance in the difference in detected stones between the plain films and computed radiographs will be performed. Stone number and composition will also be considered in the ability to detect stones.

**Progress :** 20 stones collected previous year, original data was not adequate and repeat data collection is pending.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/159		<b>Status:</b> On-going
<b>Title:</b> Magnetic Resonance Mammography (MRM)[colon] A Promising Application for Fat Suppression by Phase Unwrapping in the 3-Point-Dixon Method				
<b>Start Date:</b> 09/21/94		<b>Est. Completion Date:</b> Apr 96		
<b>Department:</b> Radiology		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Vincent B. Ho, MC				
<b>Associate Investigators:</b> J. Szumowski		Rush A. Youngberg		
<b>Key Words:</b> Magnetic Resonance Mammography: fat suppression, Dixon method				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//

**Study Objective:** The objective of this study is to further refine a promising new MRI technique for fat suppression (phase unwrapping in a 3-point-Dixon method) for application in magnetic resonance mammography (MRM).

**Technical Approach:** Phase unwrapping in the 3-point-Dixon method is a recently described method for fat suppression which promises to bridge the difficulties encountered with fat signal on post-contrast MRM images. This new fat suppression technique promises to provide the reproducible homogeneous fat suppression necessary for the efficient performance of MRM and the accurate rendering of diagnoses.

This new technique, by increasing the conspicuousness for areas of Gd-enhancement, will dramatically improve the overall accuracy of MRM for breast cancer and make the identification of even very small cancers possible. MR with its reported high sensitivity will potentially identify lesions not otherwise detected by film screen mammography, ultrasound or physical exam at MAMC, MRM has already discovered lesions which were otherwise not detected by these other conventional means. Because the success of any breast imaging modality relies on its ability to diagnose cancer early to effect cure and increase survival, this technique will represent a major advance in breast cancer screening.

**Progress :** 7 patients have been entered. Patient enrollment continues. Delay in initiation of clinical trials resulted from the 8-month delay in upgrade of MAMC MRI unit.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/181		<b>Status:</b> On-going	
<b>Title:</b> Optimizing Breath Hold Technique for MR Scanning					
<b>Start Date:</b> 09/15/95			<b>Est. Completion Date:</b> Oct 96		
<b>Department:</b> Radiology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Richard S. Makuch, MC					
<b>Associate Investigators:</b> MAJ Joseph D. Kern, MC			MAJ Vincent B. Ho, MC		
<b>Key Words:</b> MRI, breath holding					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//	

Study Objectives: To optimize a patient's ability to hold his/her breath during the performance of an MRI scan and to identify predictors for breath holding capacity prior to scanning.

Technical Approach: This is a prospective study to evaluate and optimize a patient's ability to hold his/her breath during the performance of an MRI scan. Any patient obtaining an MRI scan will be eligible. In addition, we will attempt to formulate pre-examination predictors of a patient's breath holding capabilities prior to MR scanning. Up to 500 volunteers will be selected in the following year to participate. A brief questionnaire will be filled out that will provide standard demographic data such as age, sex, social security number, etc. In addition, a quick history will be performed to ascertain the presence of smoking history, congestive heart failure, prior thoracic surgery, COPD or other pulmonary disease. Volunteers will undergo a modified pulmonary function test with a hand-held device to assess peak flow and have their oxygen saturation value recorded with a pulse oximeter. They will then be asked to perform breath hold for as long as possible in the supine-end inspiration and -end expiration and the prone-end inspiration and -end expiration positions with 2 minutes of rest between holds. The volunteers will then be coached to hyperventilate for 15 seconds on 4-6L/min of oxygen and asked to again perform breath hold in the same four positions. Results of breath holding capability will be correlated with initial oxygen saturation peak flow reading as well as demographic data. Data analysis will be accomplished by chi-square method employing the computer software Statview 4 by Abacus Concepts, Inc., Berkeley, CA.

Progress : New study, waiting for final approval.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/075		<b>Status:</b> Completed	
<b>Title:</b> Cost Effectiveness of Screening MRIs of the Knee Prior to all Knee Arthroscopies					
<b>Start Date:</b> 03/04/94			<b>Est. Completion Date:</b> Aug 94		
<b>Department:</b> Radiology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Liem T. Mansfield, MC					
<b>Associate Investigators:</b> LTC Gregg W. Taylor, MC			Rush A. Youngberg MAJ Winston J. Warme, MC		
<b>Key Words:</b> MRI, knee, arthroscopy					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> //

**Study Objective:** 1. To determine the sensitivity (SN), specificity (SP), negative predictive value (NPV), positive predictive value (PPV), and accuracy of knee MRIs in predicting internal derangement of the knee.;2. To determine the percentage of negative diagnostic knee arthroscopies.;3. To determine whether screening MRIs can reduce the number of negative arthroscopies resulting in institutional cost savings and a reduction in patient morbidity.

**Technical Approach:** This is a prospective, single-blinded study of MRI versus diagnostic arthroscopy, comparing their abilities to diagnose internal derangement(s) of the knee. Patients selected for this study will have met the surgical indications monitoring for appropriateness (SIM-A) suggested criteria for selected orthopedic surgery procedures.

Patients (100) will have an MRI of the knee prior to arthroscopy which is to be within 2 weeks after the MRI. MRIs will be interpreted by Drs. Youngblood and Mansfield. Arthroscopies will be performed by Dr. Taylor and other orthopedic senior staff. MRI interpretation will be in the form of a radiological report and a diagram showing the location of meniscal tears. The arthroscopists performing the arthroscopy will record his findings both before and after review of the radiologic findings.

Using diagnostic arthroscopy as the gold standard, after 100 arthroscopies the data will be reviewed to determine the SN, SP, NPV, PPV, accuracy of MRI, and the frequency of avoidable arthroscopy. Avoidable diagnostic arthroscopy will be defined as arthroscopy performed on a patient whose MRI and arthroscopic findings demonstrate non-surgical pathology.

**Progress :** Fifty patients underwent MRI. Despite very stringent clinical criteria in selecting arthroscopy patients, 42% of the patients could have been spared the procedure, based on MRI screening. This prospective study indicates that screening knee MRI is cost effective, resulting in a cost saving of as much as \$680 per patient.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 93/113	<b>Status:</b> Completed
<b>Title:</b> A Clinical Comparison of Nodule Detection Utilizing A Modified ROC Study[colon] Conventional vs. Digital vs. Digital-AMBER Chest Radiography		
<b>Start Date:</b> 06/09/93	<b>Est. Completion Date:</b>	
<b>Department:</b> Radiology	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Cristopher A. Meyer, MC		
<b>Associate Investigators:</b> CPT Robert Leckie, MC Jon R. Carter, M.S.		
CPT Kyle L. Colvin, MC MAJ Donald V. Smith, MC LTC William H. Cragun, MC		
<b>Key Words:</b> radiography:AMBER, digital, conventional		
<b>Accumulative</b> <b>MEDCASE Cost:</b>	<b>Est. Accumulative</b> <b>OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$224.00	//

**Study Objective:** To evaluate the efficiency of combined AMBER-Storage Phosphor Digital Radiography (AMBER-SPDR) in the detection of pulmonary nodules versus conventional radiography alone and storage phosphor digital radiography (SPDR) alone, using a modified receiver operating characteristic study.

**Technical Approach:** Patients with one or multiple pulmonary nodules, the largest measuring less than 2 cm, will be identified for inclusion by previously obtained CT. Patients will receive in addition to conventional radiography, SPDR and AMBER-SPDR chest studies. These films will be randomized and numbered. Four board certified chest radiologists and two senior residents in radiology will review the films in sets of 25/session with 75 minutes to finish each session. Each set of films will be restricted to a single modality (i.e. conventional, digital, AMBER-digital) to permit familiarity with modality and prevent inadvertent inclusion of patient images in more than one modality at the same session. All images will be viewed one at a time on standard illuminator under low ambient light conditions. A true positive is recorded if the location is within 1 cm of the center of the actual nodule.

Modified receiver operating characteristic as described by Bunch (Bunch PL, et al: A Free Response Approach to the Measurement and Characterization of Radiographic Observers Performance. J Appl Photogr Eng 1978:4,166-171.) will used to interpret the data. In this method the ordinate is the joint probability for detection and location and the abscissa is the mean number of false positive responses per image.

**Progress :** Fifty-six of the image sets have been processed. All proposed procedures are completed and data gathered. Conclusion is there is no significant difference between the 3 modalities tested using FROC methodology.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/022	<b>Status:</b> Terminated
<b>Title:</b> Free Receiver Operating Characteristic Analysis of Alveolar Consolidation Detection[colon] Conventional Chest Radiography vs. Digital Radiography vs. Digital Advanced Multiple Beam Equalization Radiography		
<b>Start Date:</b> 11/05/93	<b>Est. Completion Date:</b>	
<b>Department:</b> Radiology	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Cristopher A. Meyer, MC		
<b>Associate Investigators:</b> MAJ Robert G. Leckie, MC James H. Timmons, MD Dev P. Chakraborty, Ph.D.	LTC Bernard J. Roth, MC CPT Kyle L. Colvin, MC MAJ Donald V. Smith, MC Jon R. Carter, M.S.	
<b>Key Words:</b> AMBER, SPDR, chext x-ray, alveoli pulmonis		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** To determine the relative sensitivity of AMBER-Storage Phosphor Digital Radiography (SPDR) in the detection of alveolar consolidation by comparing AMBER-SPDR with conventional radiography using a free response receiver-operating characteristic curve.

**Technical Approach:** BAL will be performed using a flexible fiberoptic bronchoscope. Each lobe subjected to lavage will have 100 ml of saline solution instilled, followed immediately by aspiration of the infused fluid. Twenty-five patients will have one lobe lavaged, 25 patients two lobes lavages and 25 patients three separate areas lavaged. The patients will then have three follow-up posteranterior chest radiographs: a conventional radiograph, SPDR and AMBER-SPDR. Conventional chest radiographs will be performed using standard radiographic technique. Digital film will be provided in a masked, hard copy 2/3 format. Digital-AMBER films will be obtained with normal equalization and provided in a masked, hard copy 2/3 format. All digital films will be uncompressed. The films will be randomized and number. All films will be reviewed in sets of 25/session to prevent viewer fatigue and image recall. Data will be evaluated for four lung zones and a 0-4 grading system assigned for subjective level of certainty/quantification of alveolar consolidation. Analysis will be performed utilizing a free-response methodology. Spearman rank correlation will be used to determine correlation between retained lavage fluid volume and lung opacification grade.

**Progress :** This study was terminated for lack of funding.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF SURGERY, ANESTHESIA SERVICE**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/075	<b>Status:</b> On-going
<b>Title:</b> Psoas Compartment Catheter vs. PCA for Post-Operative Analgesia After Anterior Cruciate Ligament Reconstruction Surgery		
<b>Start Date:</b> 02/17/95	<b>Est. Completion Date:</b> Sep 95	
<b>Department:</b> Surgery, Anesthesia Service	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Stephen L. Bolt, MC		
<b>Associate Investigators:</b> CPT Mark C. Weston, MC		Paul J. Teiken, M.D. LTC John B. Whittemore, AN
<b>Key Words:</b> Analgesia:PO, psoas, PAC, ligament		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** To demonstrate the efficacy of single lower limb nerve plexus block for post-operative pain relief following anterior cruciate ligament (ACL) reconstructive surgery.

**Technical Approach:** All patients presenting for ACL reconstruction will receive comparable general anesthetics for their surgery. After induction of general anesthesia, the patients will be randomized into two groups for management of post-operative analgesia: a) PCA morphine alone, b) Psoas Compartment Catheter and PCA morphine. The latter group will receive a loading dose of local anesthetic through the Psoas Compartment Catheter, followed by an infusion of local anesthetic. The degree of pain relief achieved by both groups of patients will be assessed at regular intervals via : a) milligrams of morphine dispensed from the PCA pump and b) Visual Analog Pain Scale(VAPS) measurements by a disinterested investigator. We will attempt to demonstrate a 50% reduction(40mm to 20mm on the VAPS) in both postoperative pain scores and narcotic requirement in the Psoas Compartment Catheter population. The sample size is pending power analysis. The data analysis will be performed using either the Mann-Whitney test or T-test.

**Progress :** 4 patients have been enrolled in FY95. Patient accrual continues.

## Detail Summary Sheet

**Date:** 30 Sep 95      **Protocol No.:** 92/008      **Status:** Completed

**Title:** Influence of Phrenic Nerve Blockade on the Incidence of Referred Shoulder Pain in Patients Undergoing Thoracic Surgery for Pneumonectomy

**Start Date:** 12/06/91

**Est. Completion Date:**

**Department:** Surgery, Anesthesia Service

**Facility:** MAMC

**Principal Investigator:** MAJ James D. Helman, MC

**Associate Investigators:**

LTC Douglas M. Anderson, MC

COL Daniel G. Cavanaugh, MC

MAJ Edward J. Walz Jr., MC

CPT Michael J. Decker, MC

COL Michael J. Barry, MC

MAJ Frederick W. Burgess, MC

**Key Words:** referred shoulder pain, phrenic nerve

**Accumulative**

**MEDCASE Cost:** \$0.00

**Est. Accumulative**

**OMA Cost:** \$0.00

**Periodic Review:**

//

**Study Objective:** To evaluate the contribution of the phrenic nerve to the referred shoulder pain associated with thoracic surgery for pneumonectomy.

**Technical Approach:** Pneumonectomy operations may be associated with referred pain symptoms conducted by the phrenic nerve. Blockade of the phrenic nerve may inhibit these pain symptoms. This will be a double-blind randomized trial using patients greater than 18 years of age who are presenting for thoracotomy. Individuals will be assigned in a random fashion to receive either 0.9% NaCl or 0.5% bupivacaine for infiltration around the phrenic nerve above the hilum prior to closure of the thoracic cavity. There will be 8-10 patients in each group. Postoperative pain management will be provided according to standard MAMC practice with a thoracic epidural infusion of narcotic/local anesthetic. Each patient will be evaluated at 1 and 24 hours postoperatively for the presence of referred shoulder pain. Severity of pain will be assessed by the patient using a visual analog scale. Demographic data on each patient, including height, weight, age, sex, and surgical procedure will be collected and analyzed where appropriate by chi-square analysis or an unpaired t-test. Pain scores at 1 and 24 hours will be analyzed by the Mann-Whitney rank sum test. The presence or absence of referred pain will be analyzed by chi-square analysis.

**Progress :** 20 subjects entered. Reduced to absent shoulder pain post thoracic surgery as compared to pain the the placebo group.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/135	<b>Status:</b> On-going
<b>Title:</b> Epidural Pressures During Continuous Labor Epidural Infusions		
<b>Start Date:</b> 06/16/95	<b>Est. Completion Date:</b>	
<b>Department:</b> Surgery, Anesthesia Service	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ James D. Helman, MC		
<b>Associate Investigators:</b>		CPT Michael L. Pylman, MC
<b>Key Words:</b> Pressure:epidural, labor		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objectives:** To determine the pressure within the epidural space during an infusion for labor analgesia.

**Technical Approach:** Epidural pressures will be determined on 16 parturients at one hour intervals starting thirty minutes after placement of their epidural analgesia. This will be accomplished by transducing an in situ epidural catheter using a standard pressure transducer (modified wheatstone bridge). Sixteen parturients will be transduced in the right lateral decubitus position with reference to the cap of the epidural catheter during their labor. The pressure recorded will be the lowest pressure seen during the five minutes of monitoring. Univariant analysis of pressures versus time of infusion. Patient number in study chosen to give confidence interval of 95% based on standard deviation from our previous study and a projected range of 10 torr.

**Progress :** 10 subjects entered. Epidural pressures decline in patients with prolonged labor, potentially increasing the risk for entrainment of fluid and potential contamination and/or infection.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/130	<b>Status:</b> On-going
<b>Title:</b> The Effect of Lidocaine and Hydralazine on Radial Artery Flow Velocity and Diameter		
<b>Start Date:</b> 09/02/94	<b>Est. Completion Date:</b>	
<b>Department:</b> Surgery, Anesthesia Service	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT John D. Hermann, MC		
<b>Associate Investigators:</b> MAJ Stephen L. Bolt, MC MAJ James D. Helman, MC		
<b>Key Words:</b> artery:radial, artery:diameter, artery:flow velocity, lidocaine, hydralazine		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** To determine if the periarterial infiltration of lidocaine and/or hydralazine near the radial artery at the wrist will either decrease the velocity of flow and/or increase the diameter of the radial artery at the wrist as measured by a duplex/doppler instrument.

**Technical Approach:** The study will be comprised of 30 healthy volunteers recruited from the MAMC house staff. The study population will initially be comprised of 10 patients in the pilot arm of the study and an additional 20 patients will be studied to confirm the results and to improve the statistical power of the study. Each of the study subjects will serve as their own control. Prior to receiving medication the subjects will have baseline radial artery flow velocity and vessel diameter measurements made and recorded. Each of the subjects will receive the study medication in a random fashion; either normal saline; 1% lidocaine and hydralazine (2 mg/ml). The study will examine the flow velocities in the radial artery with a 5 mHz ATL Duplex scanning device before and after the infiltration of the study medication. An effort will be made to measure arterial diameter with the duplex device and compare pre and post infiltration arterial diameter. The investigators will be blinded to the type of medication being infiltrated periarterially. At the end of the study the syringe codes will be revealed and a comparison of flow velocities between the normal saline, lidocaine and lidocaine/hydralazine will be made. The percent change from baseline will be recorded for all infiltrations and the data will be analyzed using the paired T-test.

**Progress :** 10 subjects entered. First part of the study is completed and abstract was submitted to SCCM. Additional healthy volunteers are still needed.

### Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 93/082

**Status:** Terminated

**Title:** Allo-priming of Mivacurium Neuromuscular Blockade With Steroidal Nondepolarizers

**Start Date:** 04/02/93

**Est. Completion Date:** Jun 93

**Department:** Surgery, Anesthesia Service

**Facility:** MAMC

**Principal Investigator:** MAJ William A. Hughes, MC

**Associate Investigators:** None

**Key Words:** Mivacurium neuromuscular blockade:steroidal nondepolarizers

**Accumulative**

**Est. Accumulative**

**Periodic Review:**

**MEDCASE Cost:** \$0.00

**OMA Cost:** \$15.35

//

**Study Objective:** This study will evaluate the effect of a priming dose of steroidal neuromuscular blockade (NMB) on the onset and duration of mivacurium.

**Technical Approach:** Thirty patients, ASA class I or II, receiving general anesthesia for operative procedures (pilot study) will be administered an anesthetic technique limited to thiopental + narcotic induction and nitrous-narcotic maintenance. This technique is known as a "nitrous-narcotic", a common anesthetic technique. The study population will be randomly assigned to three groups of ten each: Group I (Control) will receive a priming dose of mivacurium; Group II will receive a priming dose of vecuronium; Group III will receive a priming dose of pancuronium. Each patient will be fitted with a neuromuscular blockade monitor capable of recording twitch height and time. The anesthetist will be blinded to the group assigned. A priming dose of the unknown NMB agent will be administered prior to induction. Five minutes after priming dose and induction of anesthesia, an intubating dose of mivacurium will be administered. If the duration of the procedure will not allow for spontaneous NMB recovery, then NMB will be reversed in the usual fashion (i.e., administration of neostigmine and glycopyrrolate).

Data will be analyzed for statistically significant differences in time to onset and duration of action for NMB and subsequent power analysis will determine the number of subjects needed to achieve statistical significance.

**Progress :** Lack of funds and equipment terminated this project.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/073		<b>Status:</b> Terminated	
<b>Title:</b> The Efficacy of Epinephrine as an Epidural Test Dose for Predicting Intravascular Injection During Halothane Anesthesia in Infants and Children					
<b>Start Date:</b> 03/05/93			<b>Est. Completion Date:</b> May 93		
<b>Department:</b> Surgery, Anesthesia Service			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> David M. Polaner, M.D.					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> epinephrine, halothane, infant, children					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$300.00		//	

**Study Objective:** This study will determine whether the intravenous injection of small doses of epinephrine will result in a predictable increase in heart rate during halothane anesthesia, thereby allowing "test doses" of epinephrine-containing local anesthetics to serve as an accurate and reliable marker for inadvertent intravascular injection.

**Technical Approach:** Each child will be randomized to receive either 0.75 ug/kg or 1.0 ug/kg of intravenous epinephrine after the induction of anesthesia and the establishment of a steady state of anesthesia with 1.5 MAC of halothane (adjusted for age) delivered in a 60% nitrous oxide / 40% oxygen mixture. The induction technique will be left to the discretion of the anesthesiologist as will premedication, except that patients will not receive atropine. Ventilation will be regulated to achieve an end tidal CO<sub>2</sub> concentration between 28 and 43 mm/Hg. Vital signs will be recorded continuously for three minutes using standard non-invasive techniques. Data will be analyzed using a two tailed t-test with the groups and ANOVA for repeated measures for analysis of data between the groups.

**Progress :** No subjects were entered. Study was terminated do to lack of time by the PI.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/046	<b>Status:</b> Completed
<b>Title:</b> Pressure Within the Epidural Space and Flow in Epidural Catheters		
<b>Start Date:</b> 02/17/95	<b>Est. Completion Date:</b> Jul 95	
<b>Department:</b> Surgery, Anesthesia Service	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Michael L. Pylman, MC		
<b>Associate Investigators:</b> Paul J. Teiken, M.D.		MAJ James D. Helman, MC
<b>Key Words:</b> Space:epidural, pressure:epidural		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objectives:** The objective of this study is to determine the pressure within the epidural space after an infusion for labor analgesia. This information will then be used to calculate flow in an epidural catheter at those pressures. This *in vitro* flow information can then be used to predict the behavior of fluid, as well as potential bacterial contamination, in a disconnected epidural catheter.

**Technical Approach:** Epidural pressures will be determined on healthy parturients after conclusion of their epidural infusions. This will be accomplished by transducing an *in situ* epidural catheter using a standard pressure transducer (modified wheatstone bridge). Twenty parturients, age 18-50, will be transduced in the recumbent and sitting position with reference to both the cap of the epidural catheter and the entry point of the catheter into the skin. Based on these measured pressures, *in vitro* flow calculations using a standard epidural catheter and water will be performed by placing a water reservoir with the same pressure differential to the tip of the epidural catheter as those pressures previously determined and measuring the quantity of water flowing through the catheter in 30 minutes. Numerical mean and standard deviation will be used to estimate pressures in each of the positions used. These pressures will be used for the *in vitro* phase with means and one standard deviation above and below the mean used for flow measurements.

**Progress :** Epidural pressures were positive in all patients when related to the insertion point of the epidural catheter. However, pressures were sub-atmospheric in over half of the parturients when measured at the hub of the catheter taped to the patient's shoulder when the patient was sitting. Epidural pressures also tended to lower values with increased time of infusion. Thereby, patients with prolonged labors may be more at risk for flow into the epidural space.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF SURGERY, CARDIOTHORACIC**  
**SURGERY SERVICE**

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/156		<b>Status:</b> On-going
<b>Title:</b> North American Duraflo II Working Group				
<b>Start Date:</b> 09/21/94			<b>Est. Completion Date:</b>	
<b>Department:</b> Surgery, Cardiothroacic Surgery Svc			<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Blaine R. Heric, MC				
<b>Associate Investigators:</b>			LTC Maceo Braxton Jr, MC	
<b>Key Words:</b> Duroflo II, heparin, cardiopulmonary bypass circuits				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>	
\$0.00		\$0.00	//	

**Study Objective:** To determine if Duraflo II, (a heparin surface treatment) creates in a controlled, prospective, randomized study, a more biocompatible extracorporeal environment as evidenced by the following key patient outcomes indices: (1) homologous transfusion requirements (2) post-op hours until extubation (3) post-op hours until SICU discharge (4) post-op days until hospital discharge.

**Technical Approach:** The deleterious effects of cardiopulmonary bypass on hematologic parameters have been well established in cardiac surgery. In particular, the systemic inflammatory response is a well recognized entity which occasionally may create severe clinical problems including ARDS (Adult Respiratory Distress Syndrome), neurologic dysfunction, myocardial edema and myocardial dysfunction, and postoperative weight gain.

Heparin coating all blood containing surfaces of the extracorporeal circuit creates a "pseudo endothelium". Early studies, in a relatively small number of patients in Europe, have indicated that platelet function and numbers are preserved. Bleeding is decreased. Levels of complement activation are reduced and, therefore, postoperative pulmonary function is improved. The number of patients studied in a randomized blinded fashion, however, has been very small and, therefore, improved clinical outcome using this new technology has not been documented.

The Duraflo tubing is one of several heparin coated or "biocompatible" surfaces which have been the focus of active research by many of the industries in the past several years. No U.S. center has reported a clinical evaluation of the product, despite the fact that the FDA has approved the majority of the components for use in routine clinical practice. Adding the heparin coating to the tubing increases the expense of open-heart surgery and no study has yet been able to justify its use. This will be the first study to address this question in a scientific fashion.

**Progress :** The duraflo coated oxygenator made by Baxter was not FDA approved. The study will not commence until the new duraflow coated oxygenator is available. We anticipate entry in the study starting in January 1996.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF SURGERY, OTOLARYNGOLOGY**  
**SURGERY SERVICE**



### Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 93/160

**Status:** Terminated

**Title:** Analyzing the Dynamic Behavior of the Eustachian Tube Through A Sonometric Monitor

**Start Date:** 08/06/93

**Est. Completion Date:**

**Department:** Surgery, Otolaryngology  
Surgery Service

**Facility:** MAMC

**Principal Investigator:** MAJ Charles V. Edmond Jr, MC

**Associate Investigators:** None

**Key Words:** eustachian tube, sonometric monitor

**Accumulative**

**Est. Accumulative**

**Periodic Review:**

**MEDCASE Cost:** \$0.00

**OMA Cost:** \$0.00

//

Study Objective: To develop and investigate an ambulatory monitoring eustachian tube (ET) system that will record ET events in a dynamic fashion, utilizing the technique of sonometry.

Technical Approach: This is a team approach whereby an instrument capable of dynamic testing of ET function is developed and clinically used to define the signature of selected otologic disorders and normal function. This four phase approach will utilize the capabilities of private industry and the MAMC Otolaryngology Service. Phase I will consist of fabricating and testing an improved bench top system, modeled after the Pittsburgh-Carnegie-Mellon system and will provide the formulation for the dynamic measurements. Phase II will entail development of a portable data acquisition unit which will allow the patient to wear a self contained measurement system. Upgrades will continue on the bench top system. Phase III will begin the clinical trials to investigate the dynamic nature of the ET and the characteristics of opening and closing patterns as they relate to normals and specific otologic disorders. Phase IV will emphasize the transfer of technology to a medical instrument vendor of a portable ambulatory ET monitor, that is diagnostic, user friendly, and cost efficient.

Progress : No funding for project.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/177	<b>Status:</b> On-going
<b>Title:</b> ENT Surgical Simulator Project		
<b>Start Date:</b> 09/02/94	<b>Est. Completion Date:</b> Jun 96	
<b>Department:</b> Surgery, Otolaryngology Surgery Service	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Charles V. Edmond Jr, MC		
<b>Associate Investigators:</b> Doug Sluis, Ph.D. Bill Winn, Ph.D. Don Stredney Gregory J. Wiet, MD	Dale Fawcett W. Weghorst Blake Hanaford, Ph.D. Roni Yagel, Ph.D. Bill Bolger, MD	
<b>Key Words:</b> Simulator:surgical, Simulator:ENT		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** To develop and evaluate a minimally invasive prototype surgical simulator to establish real time fidelity requirements for tactile feedback and computer image synthesis.

**Technical Approach:** This project is a two phase program with the goal of Phase I to construct a simulator prototype to serve as a platform for further enhancement and evaluation. This includes the development of the geometric and virtual database of the human sinus anatomy, the development of a system to track the surgical instruments, and the system software to implement sinuscope camera emulation and tissue dissection. The prototype will provide the novice with the ability to perform a limited sinus surgery procedure on a virtual patient using sinuscope and surgical tools similar to those used in the operating room. Visual recognition skills and psychomotor skills specific to the surgical context are improved through the experience of the simulated surgery.

In Phase II, development will continue by enhancing the simulator to include changes and enhancements suggested by surgeons in the Phase I evaluation. Additional features such as tactile feedback and tissue deformation will be integrated into the prototype as time and budget permit. During Phase II further analysis will determine the simulators training effectiveness in operation.

**Progress :** Design decisions to include system performance, performance parameters, look and feel, are in the process of being made by a project team made up of the PI and associate investigators.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/122	<b>Status:</b> On-going
<b>Title:</b> Activation of the Ras Proto-Oncogenes in Adenoid Cystic Carcinoma[colon] A Pilot Study		
<b>Start Date:</b> 03/17/95	<b>Est. Completion Date:</b> Oct 95	
<b>Department:</b> Surgery, Otolaryngology Surgery Service	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> C. A. Gutfreund		
<b>Associate Investigators:</b> R. Gomez	MAJ Robert M. Tuttle, MC MAJ Richard F. Debo, MC	
<b>Key Words:</b> Cancer:adenoid, ras proto-oncogenes		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** To determine the frequency of activation of the K-ras proto-oncogene in adenoid cystic carcinoma.

**Technical Approach:** We plan to use the polymerase chain reaction (PCR) to amplify a specific DNA segment of the K-ras proto-oncogene and then examine these PCR products for previously-described oncogenic point mutations. Specimens will be obtained from pathology specimens of histologically proven adenoid cystic carcinoma from 10 patients of any age or sex. The tissue will be recovered from paraffin blocks, prepared for PCR and amplified. The product will then be separated using agarose gel electrophoresis for size and then Southern blotted with K-ras-specific probes. This is a descriptive study and will simply determine the frequency of K-ras mutations seen in adenocystic carcinoma.

**Progress :** 10 subjects were entered at MAMC. Study is still recruiting subjects.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/040		<b>Status:</b> On-going	
<b>Title:</b> The c-myc and int-2 Oncogenes in Extracapsular Spread of Lymphatic Metastasis in Head and Neck Squamous Cell Carcinomas					
<b>Start Date:</b> 04/21/95			<b>Est. Completion Date:</b> Nov 95		
<b>Department:</b> Surgery, Otolaryngology Surgery Service			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Glen J. Mesaros, MC					
<b>Associate Investigators:</b> MAJ Charles V. Edmond Jr, MC			CPT Rodger K. Martin, MS CPT Dale T. Waldner, MC		
<b>Key Words:</b> Cancer:head and neck, oncogenes					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		//	

**Study Objectives:** To identify cases of oral cavity and oropharyngeal Squamous Cell Carcinoma (SCCA) from the Madigan tumor registry with N0,N1 without extracapsular spread, and N1 with extracapsular spread pathology. To utilize PCR technology in the retrospective genomic and gene product examination of oral cavity, oropharyngeal and nasopharyngeal SCCA. To correlate the amplification and expression of *c-myc* and *int-2* oncogene with the development of extracapsular lymphatic spread of oral cavity and oropharyngeal SCCA.

**Technical Approach:** The goal of this study is to determine whether or not an association exists between amplification and/or expression of *c-myc* and *int-2* with the presence of extracapsular spread of tumor outside the involved lymph node. The MAMC tumor registry will be searched for all tumors involving the oral cavity, oral pharynx, and hypopharynx. Specimens will be limited to 1989-1994, formalin fixed and paraffin embedded specimens which show nodal neck metastasis. A comparable number of primary tumors showing no nodal metastasis will also be incorporated and matched as to clinical staging parameters with those tumors having evidence of nodal disease. The pathology reports will then be pulled and those tumors showing extracapsular spread of tumor outside the lymphatics will be sub-categorized. The total of all specimens will be 50. The specimen blocks will be pulled, sectioned and individually reviewed by the Department of Pathology to confirm the diagnosis of SCCA and the presence or absence of extracapsular spread. Primers for mRNA PCR analysis will be derived from sequence analysis of the *c-myc* and *int-2* genes. Since these genes are not normally expressed in differentiated, non-proliferating cells, the demonstration of the expression of these two genes would be consistent with the previous findings in SCCA. If significant correlation is found between presence of the oncogene transcripts (proof of expression) and extracapsular spread, the relationship between extracapsular spread and over-expression of these genes will be explored.

**Progress :** Investigators have completed a review of medical records for selection of appropriate tumor specimens, acquired FFPE tumor specimens and confirmed diagnosis with Pathology. A portion of the tumor specimens have been studied at this time

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/101		<b>Status:</b> Completed	
<b>Title:</b> Sustained Release of Recombinant Human Transforming Growth Factor-Beta1 Enhances Healing in a Rat ( <i>Rattus norvegicus</i> , strain HSD) Incisional Wound Model					
<b>Start Date:</b> 03/24/95			<b>Est. Completion Date:</b> Sep 85		
<b>Department:</b> Surgery, Otolaryngology Surgery Service			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Thomas E. Phillips, MC					
<b>Associate Investigators:</b>			MAJ Charles V. Edmond Jr, MC		
<b>Key Words:</b> Wounds:incisional,,Animal Study					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		//	

**Study Objective:** To demonstrate that the peptide growth factor known as recombinant human transforming growth factor-beta<sub>1</sub> (rhTGF-B<sub>1</sub>) delivered via a unique system of microencapsulation in absorbable suture material will increase wound strength in a rat incision wound healing model.

**Technical Approach:** This study examines the effectiveness of delivering rhTGF-B1 topically or by microencapsulation onto absorbable suture on wound healing. Four groups of ten rats each will receive different wound closure methods. Under general anesthesia and sterile conditions, all rats will have two similar incisions made on their backs, but the wounds will closed differently according to group assignment. Group one rats will be closed using untreated absorbable suture. Group two rats will be closed using microencapsulation-treated suture without the rhTGF-B1 peptide. Group 3 will be closed using untreated suture with a topical application of rhTGF-B1. Group 4 rats will be closed using rhTGF-B1-microencapsulated absorbable sutures. At specific times, rats will be euthanitized, their wounds surgically excised, and their wound breaking strength tested and compared. The breaking strength will be plotted as a mean  $\pm$  standard error of the mean against day after wounding. P values will be derived by analysis of variance.

**Progress :** Surgery, wound harvesting, and wound strength testing have been completed on 39 of 40 experimental animals. One rat expired from complications of anesthesia.

Statistical analysis of wound breaking strength has shown significant differences between experimental groups. The strongest group had a single topical application of rhTGF-B<sub>1</sub> (not encapsulated). The wounds closed with suture encapsulated with rhTGF-B<sub>1</sub> were stronger than wounds in either control group. There was no difference between wound strength in the control groups.

The data suggest that microencapsulation into absorbable suture is an effective method of applying a growth factor into an incisional wound. More study is necessary to explain why a single topical dose at the time of wounding was more effective than a sustained release delivery.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/161		<b>Status:</b> On-going	
<b>Title:</b> Success of Preoperative Imaging and Unilateral Neck Exploration for Primary Hyperparathyroidism					
<b>Start Date:</b> 09/15/95			<b>Est. Completion Date:</b> Sep 95		
<b>Department:</b> Surgery, Otolaryngology Surgery Service			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Thomas E. Phillips, MC					
<b>Associate Investigators:</b> S.K. Clark			MAJ Charles V. Edmond Jr, MC D.W. Moore		
<b>Key Words:</b> Hyperparathyroidism, ultrasound, neck exploration					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		//	

**Study Objective:** To demonstrate that preoperative imaging with high resolution ultrasound and scintigraphy followed by unilateral neck exploration is a valid approach to the management of primary hyperparathyroidism.

**Technical Approach:** Head and neck surgeons at Swedish Hospital Medical Center, frequently assisted by otolaryngology residents from Madigan Army Medical Center, have performed over 75 neck explorations for hyperparathyroidism over the past 5 years. Their operative approach involves attempts at preoperative localization with ultrasound and nuclear imaging, followed by unilateral neck exploration. This approach is somewhat controversial and not embraced by all surgeons.

Utilizing a retrospective review of all patients' charts who have received parathyroid surgery at Swedish Hospital, with the diagnosis of primary hyperparathyroidism from January 1, 1990 through March 1995 (approximately 75 patients). We will analyze several factors. Most importantly will be long-term success of surgery as measured by maintenance of normocalcemia postoperatively. The sensitivity and specificity of the preoperative imaging as compared to operative findings and histopathology will be determined. An attempt will be made to analyze factors which may have led to treatment failures.

**Progress :** Approximately 75 inpatient records and 25 outpatient records have been reviewed to data. Compilation and statistical analysis will begin when remaining records are reviewed and any necessary follow-up data gathered.

### Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 95/050

**Status:** On-going

**Title:** A Multicenter, Randomized, Parallel Group, Evaluator Blinded, Comparative Study of the Safety and Efficacy of Ofloxacin Otic Solution and Augmentin Oral Suspension in the Treatment of Acute Purulent..

**Start Date:** 12/16/94

**Est. Completion Date:** Jul 95

**Department:** Surgery, Otolaryngology  
Surgery Service

**Facility:** MAMC

**Principal Investigator:** COL David G. Schall, MC

**Associate Investigators:**  
MAJ Ray E. Jensen, MC

MAJ Richard F. Debo, MC

**Key Words:** Otorrhea, ofloxacin, augmentin, tympanostomy tubes

**Accumulative**

**MEDCASE Cost:** \$0.00

**Est. Accumulative**

**OMA Cost:** \$0.00

**Periodic Review:**

//

**Study Objective:** To compare the safety and efficacy of ofloxacin otic solution to Augmentin oral suspension in the treatment of acute purulent otorrhea in children with tympanostomy tubes.

**Technical Approach:** This is a multicenter, randomized, parallel group, evaluator blinded study with a comparative therapy control. At least 20 investigative centers will participate. The investigators will collectively enroll approximately 320 subjects to ensure clinically evaluable data from 276 subjects. All subjects will have tympanostomy tube(s) in place and acute purulent otorrhea. Subjects will be treated for 10 days. The ofloxacin otic solution will be instilled twice daily. Augmentin oral suspension will be administered every 8 hours. Subjects will have baseline pre-therapy qualifying procedures and evaluations performed at Visit 1. All subjects will subsequently return for an evaluation at 4-6 days after initiation of treatment, 1-3 days after completion of treatment, and 7-10 days after completion of treatment. Safety evaluations will be made by assessing adverse events during the course of the study. Safety will also be based on changes in the physical examinations and vital signs performed at baseline, and all return visits. Audiometry will be an additional end point for safety. Efficacy will be based on clinical response during the study by performing outcome assessments at each visit. Bacteriological efficacy will also be evaluated. The primary efficacy parameter will be the presence or absence of otorrhea.

**Progress :** 4 subjects have been entered. Enrollment will continue through December 1995.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/051		<b>Status:</b> On-going	
<b>Title:</b> A Multicenter, Prospective With Historical and Current Practice Control, Open-Label Study to Examine the Safety and Efficacy of Ofloxacin Otic Solution in the Treatment of Purulent Otorrhea...					
<b>Start Date:</b> 12/16/94			<b>Est. Completion Date:</b> Jul 95		
<b>Department:</b> Surgery, Otolaryngology Surgery Service			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL David G. Schall, MC					
<b>Associate Investigators:</b> MAJ Ray E. Jensen, MC			MAJ Richard F. Debo, MC		
<b>Key Words:</b> Otorrhea, ofloxacin					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//	

**Study Objective:** To demonstrate the safety and efficacy of ofloxacin otic solution in the treatment of chronic suppurative otitis media with otorrhea in adolescents and adults with perforated tympanic membranes.

**Technical Approach:** This is a multicenter open-label study with an historical control arm (Historical Practice Group) and a current control arm (Current Practice Group). Documented records of Historical Practice at the same institutions for up to the prior four years will serve as the historical control. At least 15 investigative centers will participate. The investigators will collectively enroll approximately 150 subjects to ensure clinically evaluable data from 126 subjects for the ofloxacin group. Subjects will be treated for 14 days. The ofloxacin otic solution will be instilled twice daily. Subjects will be evaluated at baseline, 4-6 days after initiation of treatment, 1-3 days after completion of treatment, and 7-10 days after completion of treatment. Safety evaluations will be made by assessing adverse events during the course of the study. Safety will also be based on changes in the physical examinations and vital signs performed at baseline and all return visits. Efficacy will be based on clinical response during the study by performing clinical assessments at each evaluation. Bacteriological efficacy will also be evaluated. The primary efficacy parameter will be the presence or absence of otorrhea.

**Progress :** 1 subject has been entered. Enrollment will continue through December 1995.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/128	<b>Status:</b> Terminated
<b>Title:</b> Utility of Transtympanic Ultrasound in the Diagnosis of Middle Ear Pathology		
<b>Start Date:</b> 08/05/94	<b>Est. Completion Date:</b> Sep 94	
<b>Department:</b> Surgery, Otolaryngology Surgery Service	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Ronald E. Schwartz, MC		
<b>Associate Investigators:</b> MAJ Charles V. Edmond Jr, MC		G.J. Welle
<b>Key Words:</b> ear:pathology, ultrasound		
<b>Accumulative</b> <b>MEDCASE Cost:</b>	<b>Est. Accumulative</b> <b>OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objective:** To evaluate the efficacy of transtympanic ultrasound in evaluating middle ear pathology in the human cadaver.

**Technical Approach:** The first part of the study will involve obtaining normative data from ten unaltered temporal bones. This data will then be compared with already established normative middle ear anatomic data to insure reliability of transtympanic ultrasound. Data obtained will include: size, position and relationship of middle ear ossicles, distance from tympanic membrane to the promontory, signal characteristic of disease free middle ear cavity and extent of the middle ear that is able to be evaluated by ultrasound.;;The second part of the study will use the normative data obtained in the first part of the study and compare it to surgically altered temporal bones. The bones will be altered to mimic middle ear pathology seen in clinical practice. Middle ear disease that will be looked at include soft tissue masses, ossicular chain abnormalities, and surgically altered middle ear clefts. The final part of the study will involve true transtympanic evaluation of the middle ear space by placing the probe within the middle ear cavity and then obtaining both normative data and data obtained from pathologic specimens. This will allow us to assess whether areas inaccessible to transtympanic ultrasound are better assessed from within the middle ear cavity.

**Progress :** No patients have been entered. Terminated due to lack of patients.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/050		<b>Status:</b> Terminated	
<b>Title:</b> Supine Cephalometrics in the Evaluatin of Obstructive Sleep Apnea Syndrome					
<b>Start Date:</b> 12/17/93			<b>Est. Completion Date:</b> Dec 94		
<b>Department:</b> Surgery, Otolaryngology Surgery Service			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Thomas P. Winkler, MC					
<b>Associate Investigators:</b>			MAJ Ray E. Jensen, MC		
<b>Key Words:</b> sleep apnea, cephalometrics					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$1800.00		//	

**Study Objective:** To evaluate the upper airways of patients with obstructive sleep apnea syndrome by comparing lateral roentgenographic cephalometrics in patients in the upright position with patients in the supine, relaxed position.

**Technical Approach:** This study will assess the difference in evaluating the upper airway while the patient is lying down vs. standing. A population of 20 patients with diagnosed obstructive sleep apnea along with 20 controls will be studied. The study requires that three X-rays be obtained instead of the usual one X-ray. One film will be taken standing, one will be taken lying down with the teeth closed and one while lying down with the jaw open and relaxed. Specific measurement the cephalometrics will include: 1) the posterior airway space, 2) sell-nasion-supramentale angle, 3) soft palate length and 4) distance from the hyoid to the mandibular plane. Analysis will be by the student t-test.

**Progress :** Equipment to provide supine cephalometric x-rays is not available at this time and not projected to be available in the foreseeable future. PI has also PCS'd. Recommend protocol be terminated.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF SURGERY, GENERAL SURGERY  
SERVICE**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/098	<b>Status:</b> On-going
<b>Title:</b> A Prospective Study of Deep Venous Thrombosis (DVT) After Femoral Catheterization		
<b>Start Date:</b> 04/21/95	<b>Est. Completion Date:</b>	
<b>Department:</b> Surgery, General Surgery Svc	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Peter J. Armstrong		
<b>Associate Investigators:</b> LTC David F. J. Tollefson, MC		COL Charles A. Andersen, MC MAJ Lewis L. Low, MC
<b>Key Words:</b> Thrombosis:deep venous, catheterization		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objective:** To determine if femoral venous cannulation places critically ill patients at increased risk for deep venous thrombosis (DVT) despite routine prophylaxis. To determine the time course of this increased risk in relation to duration of femoral venous cannulation.

**Technical Approach:** A group of one hundred fifty critically ill patients in the Intensive Care Unit (ICU) at MAMC requiring central intravenous access on odd days of the month will be randomized to undergo right or left femoral venous catheterization. All patients will receive DVT prophylaxis consisting of calf pneumatic compression stockings. Patients will undergo serial duplex examinations of the bilateral iliofemoral veins: prior to catheterization; on day 1, 3, 5, and 7 post-catheterization; and, on the intervals thereafter for 4 weeks. The contralateral limb without catheter will be used as the control. The incidence of DVT in the cannulated limb and in the contralateral limb will be compared using a chi-squared analysis with a  $P < 0.05$  being statistically significant.

**Progress :** 5 patients have been enrolled. Two patients were identified with undiagnosed, untreated deep vein thrombosis at the time of attempted enrollment. Patient enrollment and data collection are on-going.

### Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 95/097

**Status:** On-going

**Title:** Abdominal Aortic Aneurysm (AAA) and Chronic Obstructive Pulmonary Disease (COPD); Is There a Relationship

**Start Date:** 04/21/95

**Est. Completion Date:** Mar 96

**Department:** Surgery, General Surgery  
Svc

**Facility:** MAMC

**Principal Investigator:** CPT Peter J. Armstrong

**Associate Investigators:**  
LTC William H. Cragun, MC

LTC David F. J. Tollefson, MC  
COL Charles A. Andersen, MC

**Key Words:** Aneurysm:abdominal aortic, COPD

**Accumulative**

**MEDCASE Cost:** \$0.00

**Est. Accumulative**

**OMA Cost:** \$0.00

**Periodic Review:**

//

**Study Objective:** To determine the association, if any, of AAA and COPD as well as potential pathophysiologic explanation

**Technical Approach:** A comparison will be made between patients with and without COPD and the incidence of AAA. Patients 50 years and older will be selected from those followed in the pulmonary, family practice or adult primary care clinics who have been determined to have COPD by screening history, spirometry and carbon monoxide diffusing capacity (DLCO). Controls will be age/sex matched without COPD. Selected participants will be evaluated by pulmonary function tests (spirometry, DLCO), serum alpha 1 anti-trypsin levels, serum elastase levels, serum cholesterol levels, ankle-brachial indices and abdominal aortic duplex. The incidence in the control and study groups will be compared through Chi-squared analysis and individual variables will be determined through student T-test.  $P < 0.05$  will be determined to be statistically significant. Patients and primary care physicians will be notified of the presence or absence of AAA, abnormal ankle-brachial indices, COPD, or hypercholesterolemia.

**Progress :** New study. No subjects entered at this time.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/105	<b>Status:</b> On-going
<b>Title:</b> Telomerase Activity and Telomere Length in Human Gastric Cancer		
<b>Start Date:</b> 06/16/95	<b>Est. Completion Date:</b> May 96	
<b>Department:</b> Surgery, General Surgery Svc	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Tommy A. Brown, MC		
<b>Associate Investigators:</b>		
MAJ William C. Williard, III, MC	CPT Wade K. Aldous, MS	
MAJ Kenneth W. Westphal, MC	CPT Raymond S. Lance, MC	
	Troy H. Patience, B.S.	
<b>Key Words:</b> Cancer:gastric, telomerase activity, telomere length		
<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	//

**Study Objective:** This study encompasses four objectives. To determine the presence or absence of telomerase activity in tumorous gastric tissue and normal tissue. To observe the average telomeric length of both tissue types to compare differences in length, hypothesizing that tumor tissue would have shorter telomeres. To quantify telomerase activity in tissues with an active enzyme. To determine the relationship, if any, between activity of telomerase and the stage and grade of gastric cancer.

**Technical Approach:** Tissue samples will be taken from 40 male and female patients undergoing surgical resection for gastric cancer. Tumors to be investigated include adenocarcinoma, gastric lymphoma, gastric carcinoid, gastric sarcomas and all other malignant and benign tumors. Tissue from the tumor and from surrounding histologically normal areas will be transferred from the Dept. of Pathology to the Dept. of Clinical Investigation. Genomic DNA will be extracted from the tissues and subjected to *Rsa*I and *Hinf*I restriction digestion. The fragments will then be separated by agarose gel electrophoresis, Southern blotted, and detected by chemiluminescence using a digoxigenin-labeled telomere probe. These will be visualized by x-ray film exposure and will provide the composite lengths of all telomeres in a cell population. Actual telomerase activity in tumorous and normal tissue will also be measured by extracting the enzyme from tissues and assaying for activity *in vitro*. The positive control is an immortalized cell line. Activity is measured by the successful incorporation of radio-labeled dGTP nucleotide into telomere repeats on a known DNA primer. The modified primers will be separated on a polyacrylamide gel and quantified by densitography. The differences in telomere length will be tested by a non-parametric T-test. Chi-square analysis will be used to test for telomerase activity assuming normal tissue has inactive enzyme and tumor tissue has active enzyme. The paired T-test will be used to quantify telomerase activity compared to positive controls and a non-parametric ANOVA will be used to determine the correlation between the amount of activity and the stages and grades of tumors.

**Progress :** No patients have enrolled in FY95. Patient accrual continues.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/106		<b>Status:</b> On-going	
<b>Title:</b> Telomerase Activity and Telomere Length in Human Breast Cancer					
<b>Start Date:</b> 06/16/95			<b>Est. Completion Date:</b> May 96		
<b>Department:</b> Surgery, General Surgery Svc			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Tommy A. Brown, MC					
<b>Associate Investigators:</b> MAJ William C. Williard, III, MC MAJ Kenneth W. Westphal, MC			CPT Wade K. Aldous, MS CPT Raymond S. Lance, MC Troy H. Patience, B.S.		
<b>Key Words:</b> Cancer:breast, telomerase activity, telomere length					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		//	

**Study Objective:** This study encompasses four objectives. To determine the presence or absence of telomerase activity in tumorous breast tissue and normal tissue. To observe the average telomeric length of both tissue types to compare differences in length, hypothesizing that tumor tissue would have shorter telomeres. To quantify telomerase activity in tissues with an active enzyme. To determine the relationship, if any, between activity of telomerase and the stage and grade of breast cancer.

**Technical Approach:** Tissue samples will be taken from 50 female and male patients undergoing surgical resection for breast cancer. All malignant and benign tumors resected during surgery will be investigated. Tissue from the tumor and from surrounding histologically normal areas will be transferred from the Dept. of Pathology to the Dept. of Clinical Investigation. Genomic DNA will be extracted from the tissues and subjected to *Rsa*I and *Hinf*I restriction digestion. The fragments will then be separated by agarose gel electrophoresis, Southern blotted, and detected by chemiluminescence using a digoxigenin-labeled telomere probe. These will be visualized by x-ray film exposure and will provide the composite lengths of all telomeres in a cell population. Actual telomerase activity in tumorous and normal tissue will also be measured by extracting the enzyme from tissues and assaying for activity *in vitro*. The positive control is an immortalized cell line. Activity is measured by the successful incorporation of radio-labeled dGTP nucleotide into telomere repeats on a known DNA primer. The modified primers will be separated on a polyacrylamide gel and quantified by densitography. The differences in telomere length will be tested by a non-parametric T-test. Chi-square analysis will be used to test for telomerase activity assuming normal tissue has inactive enzyme and tumor tissue has active enzyme. The paired T-test will be used to quantify telomerase activity compared to positive controls and a non-parametric ANOVA will be used to determine the correlation between the amount of activity and the stages and grades of tumors.

**Progress :** 2 patients have enrolled in this study. Patient accrual continues.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/107	<b>Status:</b> On-going
<b>Title:</b> Telomerase Activity and Telomere Length in Human Pancreatic Cancer		
<b>Start Date:</b> 06/16/95	<b>Est. Completion Date:</b> May 96	
<b>Department:</b> Surgery, General Surgery Svc	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Tommy A. Brown, MC		
<b>Associate Investigators:</b>		
MAJ William C. Williard, III, MC	CPT Wade K. Aldous, MS	
MAJ Kenneth W. Westphal, MC	CPT Raymond S. Lance, MC	
	Troy H. Patience, B.S.	
<b>Key Words:</b> Cancer:pancreatic, telomerase activity, telomere length		
<b>Accumulative</b> <b>MEDCASE Cost:</b>	<b>Est. Accumulative</b> <b>OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objective:** This study encompasses four objectives. To determine the presence or absence of telomerase activity in pancreatic tumor and normal tissue. To observe the average telomeric length of both tissue types to compare differences in length, hypothesizing that tumor tissue would have shorter telomeres. To quantify telomerase activity in tissues with an active enzyme. To determine the relationship, if any, between activity of telomerase and the stage and grade of pancreatic cancer.

**Technical Approach:** Tissue samples will be taken from 25 male and female patients undergoing surgical resection for pancreatic cancer. All malignant and benign tumors found during pancreatic tumor resection will be investigated. Tissue from the tumor and from surrounding histologically normal areas will be transferred from the Dept. of Pathology to the Dept. of Clinical Investigation. Genomic DNA will be extracted from the tissues and subjected to *Rsa*I and *Hinf*I restriction digestion. The fragments will then be separated by agarose gel electrophoresis, Southern blotted, and detected by chemiluminescence using a digoxigenin-labeled telomere probe. These will be visualized by x-ray film exposure and will provide the composite lengths of all telomeres in a cell population. Actual telomerase activity in tumorous and normal tissue will also be measured by extracting the enzyme from tissues and assaying for activity *in vitro*. The positive control is an immortalized cell line. Activity is measured by the successful incorporation of radio-labeled dGTP nucleotide into telomere repeats on a known DNA primer. The modified primers will be separated on a polyacrylamide gel and quantified by densitography. The differences in telomere length will be tested by a non-parametric T-test. Chi-square analysis will be used to test for telomerase activity assuming normal tissue has inactive enzyme and tumor tissue has active enzyme. The paired T-test will be used to quantify telomerase activity compared to positive controls and a non-parametric ANOVA will be used to determine the correlation between the amount of activity and the stages and grades of tumors.

**Progress :** No patients were enrolled in FY 95. Patient accrual continues.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/108		<b>Status:</b> On-going	
<b>Title:</b> Telomerase Activity and Telomere Length in Human Colorectal Cancer					
<b>Start Date:</b> 06/16/95			<b>Est. Completion Date:</b> May 96		
<b>Department:</b> Surgery, General Surgery Svc			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Tommy A. Brown, MC					
<b>Associate Investigators:</b>			CPT Wade K. Aldous, MS		
MAJ William C. Williard, III, MC			CPT Raymond S. Lance, MC		
MAJ Kenneth W. Westphal, MC			Troy H. Patience, B.S.		
<b>Key Words:</b> Cancer: colorectal, telomerase activity, telomere length					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		//	

**Study Objective:** This study encompasses four objectives. To determine the presence or absence of telomerase activity in colorectal tumor tissue and normal tissue. To observe the average telomeric length of both tissue types to compare differences in length, hypothesizing that tumor tissue would have shorter telomeres. To quantify telomerase activity in tissues with an active enzyme. To determine the relationship, if any, between activity of telomerase and the stage and grade of colorectal cancer.

**Technical Approach:** Tissue samples will be taken from 35 male and female patients undergoing surgical resection for colorectal cancer. All malignant and benign tumors of the colon and rectum found during surgery will be investigated. Tissue from the tumor and from surrounding histologically normal areas will be transferred from the Dept. of Pathology to the Dept. of Clinical Investigation. Genomic DNA will be extracted from the tissues and subjected to *Rsa*I and *Hinf*I restriction digestion. The fragments will then be separated by agarose gel electrophoresis, Southern blotted, and detected by chemiluminescence using a digoxigenin-labeled telomere probe. These will be visualized by x-ray film exposure and will provide the composite lengths of all telomeres in a cell population. Actual telomerase activity in tumorous and normal tissue will also be measured by extracting the enzyme from tissues and assaying for activity *in vitro*. The positive control is an immortalized cell line. Activity is measured by the successful incorporation of radio-labeled dGTP nucleotide into telomere repeats on a known DNA primer. The modified primers will be separated on a polyacrylamide gel and quantified by densitography. The differences in telomere length will be tested by a non-parametric T-test. Chi-square analysis will be used to test for telomerase activity assuming normal tissue has inactive enzyme and tumor tissue has active enzyme. The paired T-test will be used to quantify telomerase activity compared to positive controls and a non-parametric ANOVA will be used to determine the correlation between the amount of activity and the stages and grades of tumors.

**Progress :** 25 patients have enrolled in FY 95. A pilot study of these first 25 is being prepared. Data is projected to be complete by March 96.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/021		<b>Status:</b> Terminated	
<b>Title:</b> Immediate Post-Operative Feeding After Elective Colorectal Surgery					
<b>Start Date:</b> 11/18/94			<b>Est. Completion Date:</b> May 95		
<b>Department:</b> Surgery, General Surgery Svc			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Tommy A. Brown, MC					
<b>Associate Investigators:</b>			LTC Clifford L. Simmang, MC		
<b>Key Words:</b> colorectal surgery, PO feeding					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//	

**Study Objectives:** The objectives of this study are three fold. Number one is to determine whether patients undergoing elective open colorectal surgery are able to tolerate intake of liquid diet on postoperative day one. Number two is to determine if the use of Cisapride as a gastrointestinal prokinetic agent will increase the patient's tolerance of earlier postoperative oral intake will decrease hospital stay.

**Technical Approach:** The study will consist of three groups of 32 subjects per group for a total of 96 subjects: one control and two study groups. Both study groups will begin a liquid diet on post operative day one after elective open colorectal surgery. The diet will be supplemented in the study group A with Cisapride as pharmacological support of bowel motility. Study group B will receive a placebo. The study will be double blinded as to which patients are receiving Cisapride. The control will be placed NPO after the surgery and diet advanced after passage of flatus. The primary outcomes to be reviewed are whether patient can tolerate early post operative feeding, if the addition of Cisapride will improve tolerance and if early post operative feeding will result in decreased hospital stay. The data will be analyzed using a T test for hospital days and chi-square analysis for whether patients did or did not tolerate intake.

**Progress :** 25 patients were enrolled in FY 95. A pilot review of the first 25 patients revealed a large amount of subjectivity concerning advancement of diet among the residents caring for the patients. Although attempts were made to correct this, the revolving nature of resident physicians caring for the patients made this difficult. This protocol was terminated. The investigators will redesign a new study looking specifically at cisapride in postoperative patients. The data from the first 25 patients will not be used for future publication.

## Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 95/119

**Status:** On-going

**Title:** C-Reactive Protein in the Diagnosis of Acute Appendicitis

**Start Date:** 03/17/95

**Est. Completion Date:** Apr 95

**Department:** Surgery, General Surgery  
Svc

**Facility:** MAMC

**Principal Investigator:** CPT Mathew H. Chung, MC

**Associate Investigators:**  
CPT Donald Kim, MC

B.J. Davis  
MAJ William C. Williard, III, MC

**Key Words:** Appendicitis, C-reactive protein

**Accumulative**

**Est. Accumulative**

**Periodic Review:**

**MEDCASE Cost:** \$0.00

**OMA Cost:** \$0.00

//

**Study Objective:** To determine the negative predictive value of C-reactive protein (CRP) in an attempt to determine if the negative exploratory laparotomy rate (30%) can be significantly reduced. A secondary objective would be to calculate the cost savings of reducing the negative exploratory laparotomy rate.

**Technical Approach:** This study will attempt to better define the role, if any, of measuring CRP level in the diagnosis of acute appendicitis. It will determine if a normal CRP is a better negative predictor of appendicitis than normal serial leukocyte counts (WBC) and erythrocyte sedimentation rate (ESR). This study will include 100 subjects, 18 years and older, identified by the general surgery service with suspected appendicitis. Patients will have CRP, ESR and WBC testing during initial evaluation as routine. Those who do not undergo immediate surgery will have CRP, ESR and WBC tested again 12 hours later. The levels of CRP at both of these times and the need for surgery will be collected as data. Those who do not eventually go to surgery will be considered to have no appendicitis for data analysis.

**Progress :** Gathering required materials, will start data collect in November 1995.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/035	<b>Status:</b> On-going
<b>Title:</b> Madigan Army Medical Center Institute for Advanced Endoscopic Training Using the Pig (Sus scrofa)		
<b>Start Date:</b> 01/23/95	<b>Est. Completion Date:</b> Jan 98	
<b>Department:</b> Surgery, General Surgery Svc	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Timothy F. Deaconson, MC		
<b>Associate Investigators:</b>		
CPT Donald Kim, MC	LTC Clifford L. Simmang, MC	
MAJ David M. Watts, MC	MAJ Clifford A. Porter, MC	
MAJ William C. Williard, III, MC	LTC Patrick J. Offner, MC	
<b>Key Words:</b> Training:endoscopic, pig,Animal Study		
<b>Accumulative</b> <b>MEDCASE Cost:</b>	<b>Est. Accumulative</b> <b>OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	01/20/95

**Study Objectives:** To familiarize General Surgery residents and staff and invited surgeons from our local community with techniques in the management of advanced endoscopic-laparoscopic techniques. This would familiarize surgeons with techniques for laparoscopic procedures upon the esophagus and stomach., especially for anti-reflux procedures, and the biliary tract for cholecystectomy and common bile duct exploration and for the small intestine in colon for intestinal resection, appendectomy and colonic resection.

**Technical Approach:** This training protocol on laparoscopic and endoscopic surgical procedures will use a total of 10 pigs. Two to four pigs will be used per session with three sessions per year. The animals will be maintained on a nothing-by-mouth status for 12 hours prior to the procedures. General anesthesia will be used. The animals will be intubated, prepped and maintained on inhalant anesthesia. At the completion of the procedures, the pig will be euthanitized. During each procedure, each animal will be used for a single training episode. Maximum teaching benefit will be obtained by repeating the procedures in order that each trainee assigned to the animal may have an opportunity to perform the procedure in rotation. Critique forms will be utilized for the training and will provide evaluation of effectiveness of the course.

**Progress :** 4 animals were used for one course in Feb. 1995, twenty surgeons attended.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/022		<b>Status:</b> On-going
<b>Title:</b> The Use of Autologous Fibrin Glue to Prevent Post-operative Seromas in Patients Undergoing modified Radical Mastectomy				
<b>Start Date:</b> 11/18/94		<b>Est. Completion Date:</b> Dec 96		
<b>Department:</b> Surgery, General Surgery Svc		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Bret R. Hansen, MC				
<b>Associate Investigators:</b> CPT Daniel D. Mais, MC		LTC Patrick J. Offner, MC		
<b>Key Words:</b> Mastectomy, seroma, fibrin glue				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//

**Study Objectives:** To determine if the use of autologously donated fibrin glue can decrease the incidence of post-operative fluid collections in patients undergoing modified radical mastectomy.

**Technical Approach:** We plan to conduct a prospective, randomized study evaluating the effects of autologously donated fibrin glue on the flaps created during modified radical mastectomy in attempts to increase the adhesion of the flaps to the underlying tissue and prevent post-operative fluid collections. A total of 60 subjects will be recruited and randomized to a study group and a control group. All subjects will donate one unit of autologous blood pre-operatively. This blood will be used to provide the autologous fibrinogen for the study group. Surgeons will be given the fibrin preparation or saline to apply after mastectomy. The surgeons will be blinded as to whether they are applying fibrin glue or control saline. Drainage from the surgical area will be recorded by the subjects and a blinded evaluator will assess fluid accumulation at least weekly after drains are removed. Seroma fluids will be drained as necessary. Rates of seroma formation will be compared using chi-square analysis. The mean total amount of drain output and the mean length of time for the drains to be discontinued will also be analyzed using the Student's T test or a non-parametric test should the distribution prove to be non-Gaussian.

**Progress :** Awaiting final approval to start.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/100		<b>Status:</b> On-going	
<b>Title:</b> Gastroschisis in the Newborn Pig (Sus scrofa)[colon] Comparing Several Techniques for Conserving Fluid Loss and Maintaining Normothermia					
<b>Start Date:</b> 03/24/95			<b>Est. Completion Date:</b> Jan 95		
<b>Department:</b> Surgery, General Surgery Svc			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Randall M. Holland, MC					
<b>Associate Investigators:</b>			E.L. Paquette		
<b>Key Words:</b> Gastroschisis, fluid loss, normothermia, rabbit,Animal Study					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		//	

**Study Objective:** To examine several methods of conserving fluid loss and maintaining normothermia in new-born pigs with abdominal wall defects. This pilot study is designed for the investigators and the DCI veterinary staff to become familiar with the technical details of intubating, anesthetizing, and operating upon piglets. The data collection methods will also be examined for accuracy and practicality.

**Technical Approach:** This two-part pilot study will examine and compare several techniques for conserving fluid loss and normothermia in a new-born pig model. In the first part, one 24-48 hour old piglet will receive an intramuscular injection of telazole for sedation, be intubated and given isofluorane gas anesthesia. An incision will be made in the right lower quadrant and, using gentle palpitation, the abdominal contents will be eviscerated to the outside. For the next four hours, various methods of conserving fluid loss and maintaining normothermia will be attempted, including wrapping the abdominal contents in gauze and plastic and in plastic alone. After four hours, the piglet will be euthanitized. Part two is a repeat of part one, except that four piglets will be used and they will be assigned to one of four groups using different methods of conservation. Group one will receive no fluid or heat conservation method. Group two will have the abdominal contents wrapped in moist and then dry gauze. Group three will have the abdominal contents wrapped in gauze and then plastic. Group four will have the entire pig placed into a bowel bag up to its axilla. The temperature and weight of each pig will be taken every 15 minutes and the pigs will be euthanitized after four hours. The intent of the study is to familiarize investigators with intubation, anesthesia, and care and handling of piglets with abdominal wall defects. The values recorded will be used to determine the ranges temperature and fluid loss for a larger study which will follow.

**Progress :** 2 pigs done. Pilot study shows that our model is flawed. We plan to revise the model and redo the pilot.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/124		<b>Status:</b> Terminated	
<b>Title:</b> The Clinical Significance of Spilled Bile or Gallstones During Laparoscopic Cholecystectomy					
<b>Start Date:</b> 03/17/95			<b>Est. Completion Date:</b> Apr 95		
<b>Department:</b> Surgery, General Surgery Svc			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> J.M. McDonald					
<b>Associate Investigators:</b> V.C. Dorsch			LTC Patrick J. Offner, MC		
<b>Key Words:</b> cholecystectomy, bile, gallstones					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
<b>Periodic Review:</b>					//

**Study Objective:** To evaluate laparoscopic cholecystectomy patients, who have had intraoperative spilled bile or stones, for post-operative complications.

**Technical Approach:** This study will investigate the clinical outcome in patients with bile or gallstone spillage during laparoscopic cholecystectomy. We will enroll 100 patients of either sex, between 15 and 75 years of age, who will undergo laparoscopic cholecystectomy. The surgeon will be asked to fill out a form commenting on spillage of stones or bile, irrigation used, stone retrieval, and further use of antibiotics. Currently, when spillage occurs, surgeons are faced the decision to leave the spilled items, attempt retrieval, or proceed to an open laparotomy with little guidance on which is the best option. This study will serve to evaluate the clinical outcome of patients advantages or disadvantages of retrieval.

**Progress :** Sixty-five patients were enrolled in this study. Only 1 patient had a wound infection. Because of the number required to show a significant difference, the further continuation of accrual was deemed not feasible.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/038	<b>Status:</b> On-going
<b>Title:</b> Advanced Trauma Life Support Course Utilizing the Goat (Capra hircus)		
<b>Start Date:</b> 11/18/94	<b>Est. Completion Date:</b> Jul 97	
<b>Department:</b> Surgery, General Surgery Svc	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Patrick J. Offner, MC		
<b>Associate Investigators:</b> COL Preston L. Carter, MC LTC Clifford L. Simmang, MC		
MAJ Katherine L. Bevill, MC CPT Ronald J. Place, MC		
<b>Key Words:</b> Training protocol, goat, ATLS, Animal Study		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objective:** The objective of this training exercise is to teach physicians one safe method of performing five life-saving procedures for trauma patients.

**Technical Approach:** This training exercise will MAMC residents in the initial management of trauma patients. The physicians will practice the safe methods of performing the following life-saving procedures in the order listed: venous cut down, diagnostic peritoneal lavage, chest tube insertion, pericardiocentesis and cricothyroidotomy. The procedures will be performed after the animals are properly prepared and adequately anesthetized and for surgery. The endpoint of this training will be completion of all procedures or evidence of excessive distress or anesthetic instability. Students will be evaluated by instructors on the direct basis of psychomotor skills and verbalization of the indications, contraindications and potential complication of each procedure.

**Progress :** No ATLS courses were held during FY 95. Next course scheduled for Jan/Feb 1996.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/184	<b>Status:</b> On-going
<b>Title:</b> A Phase II Study to Evaluate LY320052 (rHb1.1) Compared to Standard Allogeneic Blood Transfusion Therapy in Elective Surgery		
<b>Start Date:</b> 09/15/95	<b>Est. Completion Date:</b> Nov 96	
<b>Department:</b> Surgery, General Surgery Svc	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Patrick J. Offner, MC		
<b>Associate Investigators:</b>		
COL Preston L. Carter, MC	MAJ William C. Williard, III, MC	
MAJ Clifford A. Porter, MC	MAJ David M. Watts, MC	
LTC William E. Eggebroten, MC	MAJ Timothy F. Deaconson, MC	
<b>Key Words:</b> Transfusion therapy, LY320052 (rHb1.1), allogeneic blood therapy		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objectives:** The objective of this study is to examine the efficacy of rHb1.1 (LY320052) as a hemoglobin-based oxygen carrier (HBOC) and colloid volume expander in patients undergoing elective surgery. The primary efficacy objective is to determine whether administration of rHb1.1 reduces the proportion of patients undergoing elective surgery who receive an allogeneic blood transfusion intra-operatively or post-operatively through 7 days post surgery. Another objective is to determine the safety of rHb1.1 compared with standard transfusion therapy.

**Technical Approach:** This is a multi-center, randomized, double-blind, active-controlled, parallel study of approximately 192 patients. Standard therapy of allogeneic blood transfusion will be used as the active control. Patients between the ages of 18 and 75 who are ASA I, II or III undergoing elective surgery with an anticipated intraoperative blood requirement of 2 to 4 units will be considered for this study. After obtaining consent, patients will be screened with a history, physical examination, and laboratory evaluation. Monitoring and data collection for this study will include pre-, intra-, and post-operative vital signs, and hemodynamic monitoring. Patients will be randomly assigned to receive either standard allogeneic transfusion or rHb1.1. Allogeneic transfusions will be packed red blood cells only, not whole blood. Patients randomized to the standard transfusion group will receive as many allogeneic units as is appropriate and those patients randomized to the rHb1.1 group may receive from 1 to up to 4 units of rHb1.1, but anything necessary over 4 will be met with standard therapy. Patients will be followed during and after surgery with examinations and blood tests at days 1, 2, 7, and 28 post surgery. Efficacy will be analyzed by measuring the number of allogeneic units after surgery for each group, the average comparative numbers of rHb1.1 units compared to standard therapy. The Lilly Statistical and Mathematic Science Department will perform the statistical analysis presented in the final report.

**Progress :** Patient accrual has not begun since protocol was just approved.

### Detail Summary Sheet

**Date:** 30 Sep 95      **Protocol No.:** 85/021      **Status:** Terminated

**Title:** Advanced Trauma Life Support Course

**Start Date:** 01/18/85

**Est. Completion Date:** Indef.

**Department:** Surgery, General Surgery  
Svc

**Facility:** MAMC

**Principal Investigator:** LTC Patrick J. Offner, MC

**Associate Investigators:**

COL Stanley C. Harris, MC

MAJ Christopher R. Kaufmann, MC

MAJ Leslie W. Yarbrough, VC

LTC William E. Eggebrotten, MC

**Key Words:** training protocol, ATLS, Animal Study

**Accumulative**

**Est. Accumulative**

**Periodic Review:**

**MEDCASE Cost:** \$0.00

**OMA Cost:** \$1600.00

06/10/94

**Study Objective:** To provide training to general surgery, emergency medicine, and family practice residents and, specifically, to teach proper management of the initial one hour following major trauma.

**Technical Approach:** During a laboratory session involving goat surgery, each student in the group will be directly involved in a hands-on performance of a venous cutdown, a cricothyroidotomy, a tube thoracostomy, peritoneal lavage, and pericardiocentesis. This course will be conducted 3-4 times/year at MAMC.

**Progress :** No ATLS courses were held during FY 95. Replaced by protocol number 95/038.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/142	<b>Status:</b> On-going
<b>Title:</b> Development of An Animal Model for a Simple Bone Cyst in the Goat		
<b>Start Date:</b> 05/26/95	<b>Est. Completion Date:</b> Jun 97	
<b>Department:</b> Surgery, General Surgery Svc	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Richard C. Rooney, MC		
<b>Associate Investigators:</b>		MAJ John D. Pitcher Jr., MC
<b>Key Words:</b> Cyst:bone, goat,Animal Study		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objectives:** Our primary objective is to devise an animal model to observe the developmental course of a simple bone cyst. We will use a goat (*Capra hircus*) as our model for the human system.

**Technical Approach:** We propose to develop an animal model and study the developmental course of a simple bone cyst. Since the lining of a simple cyst is similar to the joint lining of synovial tissue, we will test the hypothesis that the intraoperative implantation of synovium will develop into a cyst. Since human bone cysts are often cryptic until a fracture or other symptom occurs, they are not well studied. The development of such a model should facilitate many potential studies of simple bone cysts. Pre-operatively, the goats will undergo a baseline radiographic appraisal of the limbs. Five young animals less than two months old will be used to simulate a fetus when the aberrant synovial implantation of tissues is thought to occur. Under general anesthesia, a partial synovectomy will arthroscopically performed on the hip with implantation made on an adjacent bone. Post-operatively, the goats will be radiographed to appraise maturation of the bone cyst over a twenty three month period. The goats will then be euthanitized and their cyst lining analyzed and compared to that of synovium. Radiographs will be assessed by clinical means to determine development of a unicameral bone cyst. All data will be evaluated for the feasibility of the model.

**Progress :** Project has not been started yet.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/141		<b>Status:</b> On-going	
<b>Title:</b> Development of a Pig Model to Produce a Growing Fused Limb by Transferring Half of the Open Growth Plate From the Lower End of the Femur to the Upper End of the Tibia When the Tibia's Growth Plate....					
<b>Start Date:</b> 05/26/95			<b>Est. Completion Date:</b> Jun 96		
<b>Department:</b> Surgery, General Surgery Svc			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Richard C. Rooney, MC					
<b>Associate Investigators:</b> D. Sitler			MAJ John D. Pitcher Jr., MC		
<b>Key Words:</b> arthrodesis, hemi-femoral turndown, tibial replacement, Animal Study, pig					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		//	

**Study Objectives:** Our primary objective is to determine the feasibility of maintaining open physal plates in an autogenous, vascularized bone graft that has been traumatized by operative relocation. We will use a pig as our model for the human system in this pilot study.

**Technical Approach:** Research has indicated that it is possible to split the lower end of the adult femur (thigh bone), leave its vascular (blood) supply intact, and flip it upside down in order to use it as a replacement for the upper end of the tibia. We intend to develop a similar procedure in skeletally immature pigs to permit the limb to continue its normal growth while in a fused position. The technique is illustrated in the protocol. The total amount to limb growth should be normal because the growth plate is still functional at both ends of the femur. Before the procedure, the pigs will be weighed, have arteriograms and X-rays of limbs taken for status and measurement, establishing a baseline limb length. The some procedures will be performed at one, six and eleven months to assess bone growth. The animal will then be euthanitized and histologically examined. Radiographs, arteriograms, an limb length measurements will be evaluated by standard clinical means. Lengths of limbs will be measured and contralateral joints will be examined and compared to the surgical plates. The operative and non-operative limbs will be compared for parallel slopes.

**Progress :** Project has not been started yet.

## Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 95/004

**Status:** On-going

**Title:** Multicenter Comparative Study of Synercid (quinupristin/dalfopristin) versus standard therapy in the treatment of Complicated Gram positive Skin and Skin-structure Infections

**Start Date:** 10/21/94

**Est. Completion Date:** Nov 95

**Department:** Surgery, General Surgery  
Svc

**Facility:** MAMC

**Principal Investigator:** MAJ William C. Williard, III, MC

**Associate Investigators:**

CPT Peter J. Armstrong  
MAJ Brad A. Case, MC  
CPT Stefan M. Pettine, MC  
CPT Bret R. Hansen, MC

CPT Ronald J. Place, MC  
MAJ Katherine L. Bevill, MC  
CPT Mathew H. Chung, MC  
CPT Thomas K. Curry, MC  
CPT Raymond S. Lance, MC

**Key Words:** infections:skin, synercid, vancomycin, oxacillin

**Accumulative**

**MEDCASE Cost:** \$0.00

**Est. Accumulative**

**OMA Cost:** \$0.00

**Periodic Review:**

//

**Study Objective:** To evaluate the safety and therapeutic effectiveness of Synercid IV (7.5 mg/kg q 12h) versus standard therapy in the treatment of gram-positive complicated skin and skin structure infections (SSSI).

**Technical Approach:** Patients will be randomly assigned to receive either Synercid IV (7.5 mg/kg every 12 hours), or standard therapy that is based on the clinical presentation of the patient and the susceptibility pattern of the causative pathogen: either Oxacillin IV (2g q 6 hours) or Vancomycin IV (1g q 12 hours). Patients will be clinically assessed at baseline, on day 4, at the end of study treatment, and test of cure visit (14 to 28 days after treatment discontinuation). The primary efficacy parameter will be the Clinical Response determined at the test of cure assessment or when patients discontinue treatment before completing the test of cure assessment. Safety and tolerability of Synercid, oxacillin and vancomycin will be assessed using subjective patient reports, clinical evaluations and laboratory tests.

**Progress :** 8 subjects have been entered, patient accrual continues.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF SURGERY, OPHTHALMOLOGY**  
**SERVICE**

## Detail Summary Sheet

**Date:** 30 Sep 95**Protocol No.:** 95/066**Status:** On-going**Title:** A Parallel, Randomized, Double-Masked, Placebo-Controlled, Multicenter Study of the Effect of Adding 2.0% MK-507 Ophthalmic Solution to 0.5% TIMOPTIC-XE in Patients With Elevated Intraocular Pressure**Start Date:** 02/17/95**Est. Completion Date:** Apr 96**Department:** Surgery, Ophthalmology  
Svc**Facility:** MAMC**Principal Investigator:** COL Kevin J. Chismire, MC**Associate Investigators:**COL David P. George, MC  
LTC Rob A. Mazzoli, MC  
MAJ Thaddeus J. Krolicki, MC  
MAJ Eugene F. May, MC  
MAJ Roger K. George, MCMAJ Vernon C. Parmley, MC  
MAJ Anthony R. Truxal, MC  
LTC Elizabeth A. Hansen, MC  
MAJ William R. Raymond IV, MC  
CPT Keith Dahlhauser, MC  
CPT Lilia A. Fannin, MC**Key Words:** Pressure:intraocular, MK-507 Ophthalmic Solution, TIMOPTIC-XE**Accumulative****MEDCASE Cost:** \$0.00**Est. Accumulative****OMA Cost:** \$0.00**Periodic Review:**

//

**Study Objective:** 1) To determine whether 2.0% MK-507 has an additional ocular hypotensive effect when add to 0.5% TIMOPTIC-XE for 3 months in patients who have elevated IOP when on 0.5% TIMOPTIC-XE alone. 2) To collect safety data on 2.0% MK-507 given concomitantly with 0.5% TIMOPTIC-XE.

**Technical Approach:** 20 subjects will be enrolled in this parallel, randomized, double-masked, placebo-controlled, multicenter protocol. One open-label 2-week run-in period followed by a 12-week masked treatment period. IOP on Day 1 must be either  $\geq 24$  mmHg in one eye prior to TIMOPTIC-XE at 0900 (fellow eye not less than 20 mmHg) or IOP must be  $> 22$  mmHg in one eye 2 hours following TIMOPTIC-XE at 1100 (fellow eye not less than 18 mmHg). Between group comparison with regard to percent change in IOP from baseline will be made using analysis of variance techniques. The incidence rates for adverse experiences and ocular signs will be compared using Fisher exact test.

**Progress :** 11 subjects have been entered. Enrollment will end November 1995. Followup will continue through approx. February 1996.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/049		<b>Status:</b> Completed	
<b>Title:</b> A Multiple-dose, Double-masked, Active Treatment Controlled, 2 Period, Crossover Multiclinic Study of 0.5% Preservative-Free Timolol-in-GELRITE.... in Patients With Elevated Intraocular Pressure					
<b>Start Date:</b> 12/17/93			<b>Est. Completion Date:</b> Dec 94		
<b>Department:</b> Surgery, Ophthalmology Svc			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL Kevin J. Chismire, MC					
<b>Associate Investigators:</b> CPT Benjamin N. Gilbert, MC			MAJ Vernon C. Parmley, MC		
<b>Key Words:</b> Intraocular pressure, Timolol-in-Gerlite, with and without preservative					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		//

**Study Objective:** 1. To compare the relative ocular hypotensive effect of 0.5% preservative-free Timolol-in-Gelrite administered one daily to that of 0.5% Timolol in-Gelrite with preservative administered once daily.

2. To compare the safety and tolerability of both preservative-free timolol-in-Gelrite and timolol-in-Gelrite with preservative.

**Technical Approach:** Ten to twelve patients who are twenty-one years and older with glaucoma or ocular hypertension will be invited to participate at MAMC. Between 2 and 21 days prior to entry into the study all patients will have a prestudy evaluation to include, visual acuity, external and slit lamp examination, intra-ocular pressure, dilated ophthalmoscopy, visual fields and physical examination. At 1 day prior to study the patient will be examined at 0830. If the IOP (this measurement is baseline) is > 22 mgHG the patient will be able to continue. The patient will return the next day at 0830 hours, external and slit lamp examinations will be performed. The first administration of Period 1 study drug will be administered at 0900 hrs. External and slit lamp examination will be performed at 0930 hours. Goldmann applanation IOP will be performed at 1100 hrs. This same process will be repeated on days 15, 42, 77, and 84 plus all other evaluation performed at 1 day prior to study will be repeated. Period 2 will begin on Day 85 and patients will be crossed-over. The dosing and evaluation schedule remain the same and additional study days are 99, 126, 161, and 168. On days 84 and 168, a visual field exam and ophthalmoscopy will also be conducted. Data from this study will be evaluated by the sponsor.

**Progress :** Study has been completed by sponser, 10 subjects were entered at MAMC.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/070	<b>Status:</b> Completed
<b>Title:</b> Safety and Efficacy of Laryngeal Mask Airway Anesthesia for Nasolacrimal Duct Probing and Irrigation		
<b>Start Date:</b> 06/16/95	<b>Est. Completion Date:</b> May 95	
<b>Department:</b> Surgery, Ophthalmology Svc	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Lilia A. Fannin, MC		
<b>Associate Investigators:</b> LTC Rob A. Mazzoli, MC COL Thomas H. Mader, MC		MAJ William R. Raymond IV, MC David M. Polaner, M.D.
<b>Key Words:</b> Anesthesia: Laryngeal Mask Airway, Nasolacrimal duct, probing		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** To determine the safety and efficacy of laryngeal mask anesthesia for nasolacrimal duct probing and irrigation in children.

**Technical Approach:** We will retrospectively review the records of all pediatric cases of nasolacrimal duct obstruction requiring surgical intervention performed at MAMC from January 1992 to September 1994. Cases will be evaluated for the method of anesthesia used for the procedure (mask, endotracheal tube or LMA). Age, anesthetic complications, surgical complications and postoperative complications will be evaluated for each patient. We will evaluate if the LMA is associated with more complications compared to the mask and endotracheal methods. We will also determine if its ease of use is comparable to endotracheal intubation in terms of access to the eye and adnexal structures as well as airway safety. Data will be analyzed using chi-square techniques.

**Progress :** 30 subjects have been entered. The LMA was utilized in 10 cases and endotracheal intubation in nineteen. The study demonstrated that the LMA is safe and effective for use in pediatric nasolacrimal duct probing and irrigation and could be considered for use in other relatively short procedures requiring general anesthesia.

## Detail Summary Sheet

**Date:** 30 Sep 95      **Protocol No.:** 95/188      **Status:** On-going

**Title:** A Parallel, Randomized, Double-Masked Study Comparing the 0.5% Timolol/2.0% MK-0507 Combination Ophthalmic Solution BID to 0.5% Timolol Ophthalmic Solution BID or 2.0% MK-0507 Ophthalmic Solution ...

**Start Date:** 09/15/95

**Est. Completion Date:** Nov 96

**Department:** Surgery, Ophthalmology  
Svc

**Facility:** MAMC

**Principal Investigator:** MAJ Roger K. George, MC

**Associate Investigators:**

MAJ Vernon C. Parmley, MC

MAJ William R. Raymond IV, MC

COL David P. George, MC

MAJ Eugene F. May, MC

MAJ Anthony R. Truxal, MC

COL Kevin J. Chismire, MC

LTC Rob A. Mazzoli, MC

CPT Gregory S. Witkop, MC

LTC Elizabeth A. Hansen, MC

MAJ Peter G. Torok, MC

CPT R. Kevin Winkle, MC

**Key Words:** IOP, Timolol, MK-0507

Accumulative	Est. Accumulative	Periodic Review:
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	//

**Study Objectives:** To compare the intra ocular pressure (IOP)-lowering effect of the 0.5% timolol/2.0% MK-0507 combination to that of 0.5% timolol and to that of 2.0% MK-0507 for up to 3 months. To compare the safety profile of the 0.5% timolol/2.0% MK-0507 combination to that of its components administered as in their usual monotherapy dose regimens over a 3-month period.

**Technical Approach:** This is a parallel, randomized, double-masked, active-controlled study. A 3-week, open-label timolol run-in period will be followed by a 12-week masked treatment period. Two hundred forty patients with an open-angle glaucoma or ocular hypertension will be entered into the study to obtain at least 200 evaluable patients who complete the 12 week masked period. Patients will be randomized 2:2:1 to receive either the combination b.i.d. + placebo q.d., timolol b.i.d. + placebo q.d., or MK-0507 t.i.d., respectively. It is hypothesized that the test combination and dose of timolol/MK-0507 will have a lowering effect greater than each of its components. The evaluation requires statistical comparisons between the combination and each component. Analysis of variance will be used to evaluate this using the percent change in IOP from the time matched baseline at the Day 90 Hour 0 exam. The ANOVA model will include terms for treatment, clinic and treatment-by-clinic interaction.

**Progress :** Has not begun, pending MEDCOM approval.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/127	<b>Status:</b> On-going
<b>Title:</b> Army Aviation Vision Standards Research[colon] The Incidence of Refractive Anomalies in US Army Pilots		
<b>Start Date:</b> 05/19/95	<b>Est. Completion Date:</b> Sep 95	
<b>Department:</b> Surgery, Ophthalmology Svc	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Steven C. Hadley, MC		
<b>Associate Investigators:</b> COL Thomas H. Mader, MC		W.J. Hubicki Troy H. Patience, B.S.
<b>Key Words:</b> Refractive anomalies, Army pilots		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

Study Objective: Our objective is to determine the incidence of refractive anomalies in the US Army pilot population.

Technical Approach: Flight physicals are required annually on all active duty (AD), reserve (Res.) and National Guard (NG) aviators IAW AR 600-105. All flight duty medical exams (FDME) are submitted to the Army Aviation Center at Ft. Rucker, AL for approval and data collection. Fort Rucker maintains copies of all flight physicals. Approximately 20,000 class one (initial entry into aviation service) and class two (annual renewal) FDME are submitted each year. Seven years ago, Ft. Rucker started to electronically store all data from the FDME including visual acuity and refraction. We plan on utilizing the data repository at Ft. Rucker to determine the incidence of refractive anomalies in the AD, Res., and NG pilots in the US Army. Department of the Army civilian and contract aviators will be excluded from the study.

Progress : 24 subjects were entered. Early modern cataract surgery and intraocular lens implantation is a viable procedure to maintain flight status and correct military aviators visual loss due to cataract.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/061	<b>Status:</b> Completed
<b>Title:</b> Duration of Pressure Lowering Effect Utilizing Preoperative Intraocular Pressure Reduction Device		
<b>Start Date:</b> 01/20/95	<b>Est. Completion Date:</b> Apr 95	
<b>Department:</b> Surgery, Ophthalmology Svc	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Steven C. Hadley, MC		
<b>Associate Investigators:</b> MAJ Anthony R. Truxal, MC MAJ Thaddeus J. Krolicki, MC		
<b>Key Words:</b> Itraocular pressure, reduction device, duration of effect		
<b>Accumulative</b> <b>MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative</b> <b>OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Objectives:** Our objective is to determine if the bel efrit of mechanical preoperative intraocular pressure (IOP) reduction, which is an accepted part of cataract surgery, has duration to benefit the surgery.

**Technical Approach:** This study will evaluate the duration of mechanical intraocular pressure reduction. IOP pressure reduction is usually completed preoperatively to reduce positive vitreous pressure and its associated complications. Due to sterile surgical preparation, the IOP reducer is usually removed 10 - 20 minutes prior to intraocular entry. We will attempt to validate or invalidate the use of IOP reducers preoperatively . We hypothesize that the IOP reduction is short term and the IOP returns to normal or almost normal prior to intraocular penetration. If this is true, the benefits of IOP reduction preoperatively is not from straight mechanical IOP control.

Sixteen volunteer non glaucomatous patients will have baseline IOP measured in both eyes. Following baseline measurement, a McIntyre Oculo-Pressor will be applied to one eye for 15 minutes to reduce the intraocular pressure. The IOP will be evaluated after removal of the IOP reducer and every 2.5 minutes subsequently for 20 minutes. The fellow eye will be used as a control.

A power analysis was performed, assuming intraocular pressure range of 10-22 mm Hg, mean of 17, standard deviation of 2.5 mm Hg and a significant IOP reduction of 5.0 mm Hg. The required sample size (one tailed T-test - IOP reduction only) was 12 subjects.

**Progress :** 16 subjects entered. It was discovered that pressure lowering effect is transient and eye returns to normal pressure within 12 minutes.

## Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 94/112

**Status:** Completed

**Title:** Clinical Utility and Reliability of Afferent Pupillary Defect Testing

**Start Date:** 06/03/94

**Est. Completion Date:** Jun 94

**Department:** Surgery, Ophthalmology  
Svc

**Facility:** MAMC

**Principal Investigator:** MAJ Eugene F. May, MC

**Associate Investigators:**  
CPT Benjamin N. Gilbert, MC

CPT Curtis S. Hansen, RPH, MSC

**Key Words:** afferent pupillary defect, visual acuity, color vision, contrast sensitivity, visual field defect

**Accumulative**

**Est. Accumulative**

**Periodic Review:**

**MEDCASE Cost:** \$0.00

**OMA Cost:** \$0.00

//

**Study Objective:** The goal of the study is to determine the clinical utility of a recently described method of quantification of the afferent pupillary defect (APD), by comparing the amplitude of the APD with other standardized measures of optic nerve function. In addition, individual physician's measurements of APD amplitude will be compared to other physicians' measurements to assess interrater variability.

**Technical Approach:** This study will measure the amplitude of the APD in a series of 60 outpatients with optic neuropathies using the technique of Bell et al. The amplitude of the APD measured as such in each patient will be compared to a similar measurement using the neutral density filter technique. Each patient will also undergo visual acuity, color sensitivity, contrast sensitivity, and visual field testing. The following examiners will perform APD testing on each patient without knowledge of the others' results: a neuro-ophthalmologist, a general ophthalmologist, and an ophthalmology resident. Only the neuro-ophthalmologist will be familiar with each patient's history. For each examiner, a regression analysis will be performed between the APD amplitude using the neutral density filter and the APD grade using the technique of Bell et al to determine the accuracy of the new technique compared to the "gold standard". In addition, regression analysis will be performed between the visual function tests and the APD grade and amplitude for each examiner, in all patients, to assess the relationship of each measurement to the more standard tests of vision. The results from each examiner using each technique will be compared to the results from the other examiners (using kappa statistic and repeated measures ANOVA) to assess reliability of the measurement.

**Progress :** Fifty-two subjects were enrolled in this study. Forty-eight patients underwent RAPD grading using the neutral density filter technique (NDF) and the variation of the swinging flashlight test (SFT) described in the protocol. Each patient underwent extensive vision function testing. Conclusions are that RAPD quantification using the NDF technique is more reproducible than the SFT. However, there is enough variability with either test that a difference in RAPD grade obtained by different examiners may not reflect a change in the patient's clinical status. RAPD grade using either technique is well correlated to difference in mean deviation of the visual field of each eye.

## Detail Summary Sheet

**Date:** 30 Sep 95      **Protocol No.:** 94/125      **Status:** On-going

**Title:** Efficacy of Detection of Intraocular and Intraorbital Plastic Foreign Bodies by Magnetic Resonance (MR) and Computed Tomography (CT) Imaging in the Goat

**Start Date:** 06/10/94      **Est. Completion Date:** Apr 95

**Department:** Surgery, Ophthalmology Svc      **Facility:** MAMC

**Principal Investigator:** LTC Rob A. Mazzoli, MC

<b>Associate Investigators:</b>	CPT Lilia A. Fannin, MC
COL Thomas H. Mader, MC	MAJ Vernon C. Parmley, MC
COL David P. George, MC	MAJ Vincent B. Ho, MC
MAJ Miquel J. Rovira, MC	W.F. Coughlin

**Key Words:** Foreign bodies:intraocular, Foreign bodies:intraorbital, Foreign bodies:plastic, MRI, CT scan,Animal Study

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	//

**Study Objective:** 1. To determine the efficacy of CT and MR imaging in detecting intraocular or intraorbital plastic foreign bodies in the goat.;2. To determine if intravenous contrast during CT and MR imaging improves the detection of intraocular or intraorbital plastic foreign bodies.

**Technical Approach:** Twelve goats will be used to evaluate the efficacy of CT and MR imaging in detecting plastic foreign bodies in the eye and around the eye. The goats will be sedated, anesthetized, and intubated prior to the surgical placement of 1 to 6 plastic foreign bodies (sizes ranging from 1/32 - 1/4 inch) in the eye. The wound will not be closed so as to simulate an eye injury. Plain film x-ray, CT and MR images will be obtained. Intravenous dye will be given for the imaging studies. The fellow eye will be the control. After the CT and MR studies are completed, the goats will be sacrificed. Plain films, CT and MR images will be evaluated by four masked physicians (two radiologist and two ophthalmologists). These doctors will not know which eye has the plastic foreign bodies. From these evaluations, we will determine if CT or MR are equally effective in detecting the foreign bodies and we will determine if the intravenous dye improved the detection of the plastic foreign bodies.

**Progress :** Twelve animal models have been studied, scanned and harvested for specimens. Scans are being reviewed by various blinded observers (Ophthalmology and Radiology). Analysis is still on-going.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/178	<b>Status:</b> On-going
<b>Title:</b> Assessment of Post-operative Healing Time and Induced Astigmatism when Penetrating Keratoplasty is Performed Using the Tampa Trephine versus the Traditional Hanna Trephine		
<b>Start Date:</b> 09/15/95	<b>Est. Completion Date:</b> Oct 97	
<b>Department:</b> Surgery, Ophthalmology Svc	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Vernon C. Parmley, MC		
<b>Associate Investigators:</b> CPT R. Kevin Winkle, MC		COL Thomas H. Mader, MC
<b>Key Words:</b> Keratoplasty, trephine:Tampa, trephine:Hanna, astigmatism, healing		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objectives:** To assess post-operative healing time and speed of visual recovery when penetrating keratoplasty (PK) performed by a newly developed corneal trephine (Tampa trephine) is compared with a traditional corneal trephination (Hanna Trephine).

**Technical Approach:** Sample population for both Tampa and Hanna trephination will be drawn from the cornea clinic of the Ophthalmology Service. For an alpha of 0.05 and a beta of 0.2, a sample size of 10 patient per group will be needed to detect an astigmatic difference of 2.00 diopters with an anticipated S.D. of 1.5 diopters. Patients examined and found eligible for inclusion into the study will receive informed consent and be randomly assigned by the unmasked participant to either the Tampa or Hanna group. Patients meeting the criteria for PK but not wishing to participate in the study will undergo conventional PK with the Hanna trephine. The data will not be included in analysis. After PK, patients in the study will be examined on a scheduled post-operative protocol for the first year after surgery. A nonsurgical (blinded) participant will collect astigmatic and visual acuity data for comparison. The surgeon examining the patients will know which trephine was used because examination by slit lamp biomicroscopy makes it apparent. Statistical significance tests will be selected according to specific data analyzed, either independent means T-test and confidence intervals for equal time point analysis of quantitative variables, or Fischer's exact test for equal time point of percentages of qualitative variables.

**Progress :** This study is awaiting CIRO approval.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/163		<b>Status:</b> On-going	
<b>Title:</b> The Effects of Weight Lifting and Intraocular Pressure					
<b>Start Date:</b> 07/21/95			<b>Est. Completion Date:</b>		
<b>Department:</b> Surgery, Ophthalmology Svc			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT R. Kevin Winkle, MC					
<b>Associate Investigators:</b> K.F. Dahlhauser			CPT Tamara D. Lauder, MC		
<b>Key Words:</b> Intraocular pressure, weight lifting					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		//

**Study Objective :** To describe changes in intraocular pressure (IOP) that occur while lifting weights with and without performing the valsalva maneuver.

**Technical Approach :** We will select a single study group of 40 individuals between the ages of 20 to 65 years of age who have no history of ocular disease or major cardiac disease to participate in our study. The evaluation of the patients will take place during two or three sessions. During the first evaluation, the participants will undergo baseline intraocular pressure measurements followed by determination of their one-repetition maximum (ARM), i.e., the highest weight that a subject can lift through the full range of joint motion one time only. At the other sessions, the subjects will lift a series of submaximal weights calculated at different percentages of their previously determined ARM. The submaximal weights lifted will be categorized into four percentages, to make the data more realistic and useful for a real life situation, i.e., 25%, 50%, 75%, and 100%. Also during this session, IOP measurements will be obtained prior, during, and immediately following the exercise, and 10 minutes after the exercise. IOP instillation of topical anesthetic. Changes in IOP will be correlated with the submaximal range of weight lifted that produced the change. The data obtained will then be useful clinically, for postoperative patient instruction.

**Progress :** Study has just begun with 4 subjects enrolled so far.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/164	<b>Status:</b> On-going
<b>Title:</b> Refractive Changes Due to Hypoxia Following Radial Keratotomy Surgery		
<b>Start Date:</b> 07/21/95	<b>Est. Completion Date:</b> Oct 95	
<b>Department:</b> Surgery, Ophthalmology Svc	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT R. Kevin Winkle, MC		
<b>Associate Investigators:</b> MAJ Lawrence J. White, MC		COL Thomas H. Mader, MC MAJ Vernon C. Parmley, MC
<b>Key Words:</b> Keratotomy, hypoxia		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objective :** To observe changes in corneal shape and visual acuity that may take place in subjects one year following radial keratotomy when these individuals' corneas are exposed to a low oxygen tension environment.

**Technical Approach :** Two study groups will be used for our experiment. The first study group will consist of volunteers who have had radial keratotomies. We will study several ocular parameters on these individuals, both prior to corneas exposure to hypoxia and after one or two hours of corneal exposure to pure nitrogen via a goggle apparatus. These parameters include cycloplegic refraction, intraocular pressure, corneas video keratometry, and central corneas thickness. The second study group will consist of an equal number of myopic military personnel used as controls, in whom the same aforementioned parameters will be monitored both pre and post corneas exposure to a hypoxia environment.

**Progress :** Study has just begun with no subjects yet enrolled.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/171	<b>Status:</b> Completed
<b>Title:</b> A Comparison of the Ability of Extracapsular Cataract Extraction Versus Phacoemulsification to Assist in the Control of Glaucoma		
<b>Start Date:</b> 09/02/94	<b>Est. Completion Date:</b>	
<b>Department:</b> Surgery, Ophthalmology Svc	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Gregory S. Witkop, MC		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> glaucoma, cataract extractiion, phacoemulsification		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** A retrospective comparison of the ability of phacoemulsification versus standard extracapsular cataract extraction (ECCE) to lower intraocular pressure in glaucoma patients.

**Technical Approach:** This study is a retrospective chart review from a private practitioner's office to compare the effects of two types of cataract surgery on the control of glaucoma. Inclusion criteria included, 1) well controlled glaucoma defined as minimal visual field and optic nerve head damage and an intraocular pressure considered adequate to prevent further damage, 2) having the cataract extraction performed by the same surgeon, 3) no pre- or post-cataract extraction glaucoma surgery of any kind, 4) a minimum of one year follow-up.

**Progress :** A statistically significant difference was found in post-operative outcome and number of medications needed for glaucoma control.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/113		<b>Status:</b> Completed	
<b>Title:</b> Prevalence Study of Trachoma in Uganda					
<b>Start Date:</b> 04/21/95			<b>Est. Completion Date:</b> Jul 95		
<b>Department:</b> Surgery, Ophthalmology Svc			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Gregory S. Witkop, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Trachoma, Uganda					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//	

**Study Objective:** To study the prevalence of trachoma in the Bosaga region of Uganda to determine the need for a public health and treatment program in the region.

**Technical Approach:** As part of a primary care medical mission, patients will be screened using the WHO classification of trachoma during their exam for their presenting non-ocular complaint. The WHO system was developed for nonmedical personnel. However, in our study the exams will be performed by 3 MDs and a RN. In addition, each examiner will be tested with standard photographs to establish observer reliability. Since the exam will be part of the standard physical in a primary care setting, we should not have the inherent biasing of populations caused by purely ophthalmologic screening and treatment. Therefore, each patient will be considered as a random sample. The medical mission will travel to at least one village in each of the three districts comprising the Basoga region of Uganda. Specifically, these include Nawangoma, Iganga, Kamuli, and Lawonda for a sample population of 11,000. We will examine approximately 400 patients per village for a sample size of 1200. The data will include the patients age, sex and presence or absence of each of the five markers of trachoma for each eye. The prevalence of each sign will be calculated and grouped by age and sex.

**Progress :** 1500 subjects were entered. 5% TF, 7% TI, and 10 % corneal scarring.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/045	<b>Status:</b> Completed
<b>Title:</b> Optic Nerve Impingement[colon] An Anatomic Limitation of Glaucoma Drainage Devices		
<b>Start Date:</b> 03/17/95	<b>Est. Completion Date:</b> Jan 95	
<b>Department:</b> Surgery, Ophthalmology Svc	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Gregory S. Witkop, MC		
<b>Associate Investigators:</b> COL David P. George, MC COL Kevin J. Chismire, MC		
<b>Key Words:</b> glaucoma, optic nerve		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objectives:** Our objective is to determine if a recently-revealed autopsy case, where a correctly-placed Ahmed valve was within 1 mm of the optic nerve, was an anomaly or a consistant finding which would be hazardous for glaucoma patients.

**Technical Approach:** We will obtain 25 eyebank eyes, inflate them to physiologic pressure and measure the limbus to optic nerve distance in the superonasal and superotemporal quadrants. A Student's T-test for unmatched pairs will then be performed to determine if there is staistically significant difference between the two quadrants.

**Progress :** 25 subjects were entered. A clinically significant difference between the SN and ST quadrants was found. In order to decrease the risk of ON or posterior ciliary artery impingement, glaucoma surgeons should consider this difference when selecting a device and quandrant for implantation.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF SURGERY, ORTHOPEDICS SERVICE**

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/089		<b>Status:</b> On-going	
<b>Title:</b> A Randomized Open-label, Parallel Group Comparison of the Safety and Efficacy of Lovenox (Enoxaparin) Injection versus Coumadin (Adjusted Dose Warfarin) in the Prevention of Thromboembolic Disease....					
<b>Start Date:</b> 04/01/94			<b>Est. Completion Date:</b> Jun 94		
<b>Department:</b> Surgery, Orthopedics Service			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Barry T. Bickley, MC					
<b>Associate Investigators:</b> MAJ John D. Pitcher Jr., MC			LTC Gregg W. Taylor, MC J.T. Steedman		
<b>Key Words:</b> thromboembolism, hip replacement, Lovenox, Coumadin					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		08/18/95

**Study Objective:** 1) To evaluate the safety and efficacy of Lovenox Injection versus adjusted dose Coumadin in the prevention of clinically significant thromboembolic disease following elective total hip replacement during hospitalization.

2) To determine the medium term incidence (three months post-hospital discharge) of morbidity and mortality resulting from thromboembolic disease following elective total hip replacement surgery in patients treated with Lovenox Injection vs. adjusted dose Coumadin.

**Technical Approach:** This study is divided into two phases; an inpatient period following surgery, not to exceed 14 days, and an outpatient follow-up period of three months.

This is a randomized, open-label, parallel group, multicenter study conducted in patients 18 years of age or older undergoing elective unilateral primary hip replacement. When the surgeon is satisfied that hemostasis has been achieved, and within 24 hours postoperatively, patients will begin their randomly assigned treatment of either Lovenox Injection 30 mg b.i.d. or adjusted dose Coumadin until hospital discharge, but not to exceed a maximum of fourteen (14) days. (Coumadin may be started up to 48 hours preoperatively at the discretion of the investigator.) Thereafter, all patients will return to the investigator for follow-up examinations at approximately six weeks and twelve weeks post hospital discharge.

The primary efficacy parameter will be the incidence of symptomatic thromboembolic disease during hospitalization and over the subsequent three month period.

**Progress :** 19 patients were enrolled in FY95. Patient accrual continues.

### Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 95/110

**Status:** On-going

**Title:** A Multicenter Study of Treatment of Growth Arrest by Excision of Physeal Bars

**Start Date:** 04/21/95

**Est. Completion Date:** Dec 95

**Department:** Surgery, Orthopedics Service

**Facility:** MAMC

**Principal Investigator:** MAJ Clyde T. Carpenter, MC

**Associate Investigators:** None

**Key Words:** Growth, physeal bars, excision

**Accumulative**

**Est. Accumulative**

**Periodic Review:**

**MEDCASE Cost:** \$0.00

**OMA Cost:** \$0.00

//

**Study Objective:** To perform a multi-center, retrospective collection of data on the treatment of deformities arising from growth arrest by the excision of physeal bars bones.

**Technical Approach:** This preliminary retrospective study will include all patients having had a physeal bar excision and a minimum of two years follow-up. Information collected will include: (1) age, sex, race and body habitus of the patients; (2) etiology, bone involved, placement, age, and size of the bar; and (3) the degree of angular deformity and limb length discrepancy existing prior to excision of the bar. Separate forms will be used to document the specifics of surgical intervention, any subsequent interventions, and to determine results at the end of the follow-up period. Each patient will be analyzed in terms of his/her outcome. The information collected will be used to determine the methods of treatment most often yielding acceptable results in specific situations. Student's T test, Chi-square evaluation of four fold tables, regression analysis or other statistical methods will be utilized as appropriate depending on the nature of the retrospectively collected data.

**Progress :** 50 subjects entered, seeking to enroll more subjects. Results to date presented to Pediatric Orthopedic Society of North America Annual Meeting.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/081		<b>Status:</b> Terminated	
<b>Title:</b> Postarthroscopy Analgesia Following Intra-articular Morphine and Bupivacaine					
<b>Start Date:</b> 04/02/93			<b>Est. Completion Date:</b> Mar 94		
<b>Department:</b> Surgery, Orthopedics Service			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Steven M. Crenshaw, MC					
<b>Associate Investigators:</b> CPT Patrick J. Fernicola, MC			CPT Gary D. Gridley, MC MAJ John D. Pitcher Jr., MC		
<b>Key Words:</b> Postarthroscopy Analgesia:morphine and bupivacaine					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$21.00	//	

**Study Objective:** To determine the effectiveness of intra-articular morphine when combined with bupivacaine compared to bupivacaine alone for post arthroscopy analgesia.

**Technical Approach:** Over 100 patients undergoing knee arthroscopy will receive an injection of a 30 ml solution into the knee, consisting of either 100 mg of bupivacaine with 5 mg of morphine or 100 mg of bupivacaine alone. Post operative assessment will begin in the post-anesthesia care unit and continue on the ward. These assessments will include a graded pain scale to be filled out at set intervals by the patient or health care provider. The contents of the injection will remain unknown until the study is completed. Supplemental analgesics required for pain will be recorded.

The pain scores and supplemental medications will then be analyzed to determine statistical correlation to the injection given by the ANOVA test.

**Progress :** Of the original 100 subjects planned only 20 were entered. The protocol has been terminated, and the data are too sparse to try to analyze.



### Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 94/176

**Status:** On-going

**Title:** Computer Assisted Measurement of Scoliosis from Digitized Radiographs versus Traditional Cobb Angle Measurement

**Start Date:** 12/17/93

**Est. Completion Date:** Sep 93

**Department:** Surgery, Orthopedics  
Service

**Facility:** MAMC

**Principal Investigator:** MAJ John W. Dietz, MC

**Associate Investigators:**  
MAJ Donald V. Smith, MC

LTC Richard W. Kruse, MC

**Key Words:** scoliosis, computer assisted measurements

**Accumulative**

**Est. Accumulative**

**Periodic Review:**

**MEDCASE Cost:** \$0.00

**OMA Cost:** \$500.00

//

**Study Objective:** The purpose of this study is to determine the interobserver and intraobserver error and accuracy of measurement in determining Cobb angle measurements of scoliosis and kyphosis using the digitized radiographs and measuring techniques available in the Medical Diagnostic Imaging System.

**Technical Approach:** In the first phase fifty anterior-posterior or posterior-anterior spine radiographs will be collected in the Orthopaedic Clinic by two of the Investigators. These radiographs must demonstrate coronal plane deformity of 10 degrees or more. During this the radiographs will be modified to obscure the patients' names and copy the radiographs into the MDIS system. Each radiograph MDIS image will be assigned a random number. The MDIS image and its corresponding radiograph will have different numbers and a log will be created showing which random numbers have been assigned to corresponding images. The examiners will be blinded to this information.

The images will be measured in random order. All measurements will be made using the Cobb method. A line will be drawn along the superior end plate of the upper vertebra to the inferior end plate of the lower vertebra. Some radiographs will have 2 measurable curves. Only one curve from the thoracic and one from the lumbar area will be measured. Measurements on radiographs will be done with pencil and protractors usually employed in the Orthopaedic Clinic. Measurements on MDIS images will be done by choosing lines along end plates with the mouse and indicator. Actual measurements will be made by each of four observers. Measurements will be recorded on a data sheet.

**Progress :** 30 subjects have been entered. Digitalized images are being placed in a database limiting factor is result time. The final steps only involve data collection without patient contact. The x-rays are complete.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/082	<b>Status:</b> On-going
<b>Title:</b> Comparison of Sterile Isotonic Saline, Purified Water, and Dilute Hypochlorite Solution on the Rates of Infection and Tissue Response in Open Fractures of a Syrian Hamster Model		
<b>Start Date:</b> 03/24/95	<b>Est. Completion Date:</b> Oct 96	
<b>Department:</b> Surgery, Orthopedics Service	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Randall K. Hildebrand, MC		
<b>Associate Investigators:</b> LTC Frederic L. Johnstone, MC MAJ Mark D. Brissette, MC		
<b>Key Words:</b> Fractures, saline, purified water, hypochlorite, infection, tissue response, Animal Study		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** 1) To compare different irrigating solutions and rates of infection in an open fracture model. 2) To compare the gross and histologic effects in wound healing of an open fracture model after different irrigation solutions.

**Technical Approach:** A total of 48 syrian hamsters will be used in a 4 groups of 12. There will be 3 treatment groups and one control group. After adequate anesthesia, an incision on a hamster's leg will be made and the thighbone will be broken with a small power saw. The animals will be deliberately infected, and the treatment group animals will have the wound washed out with one of several kinds of irrigating fluids (sterile isotonic saline, purified water, or dilute hypochlorite solution). The animal will be awaked from anesthesia and returned to a recovery cage to be monitored for pain or infection. Two weeks later it will be euthanized. The rates of infection will be compared and the tissue around the wound will be examined under a microscope to determine any potential harmful effects of the infection or irrigation fluid.

**Progress :** Hamsters have been ordered. Full budget of animals to be done in June 1996.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/142		<b>Status:</b> On-going	
<b>Title:</b> Cost Effectiveness of Screening MRIs of the Shoulder Prior to Neer Acromioplasties					
<b>Start Date:</b> 08/05/94			<b>Est. Completion Date:</b>		
<b>Department:</b> Surgery, Orthopedics Service			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Randall K. Hildebrand, MC					
<b>Associate Investigators:</b>			MAJ John D. Pitcher Jr., MC		
<b>Key Words:</b> acromioplasty, MRI, cost effectiveness					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		//	

**Study Objective:** 1. To determine the sensitivity (SN), negative predictive value (NPV), and positive predictive value (PPV) and accuracy of shoulder MRIs in predicting rotator cuff tears of the shoulder. 2. To determine whether screening shoulder MRIs in patients with impingement syndrome is helpful and cost effective in the surgical management of preoperative management of those cases that are refractory to non-operative treatment.

**Technical Approach:** This is a prospective, single-blinded study of MRI vs operative evaluation, comparing their abilities to diagnose rotator cuff tears and other pathology about the shoulder. Patients selected for this study will have met the surgical indications for a modified Neer Acromioplasty for impingement syndrome with or without a suspected rotator cuff tear.

One hundred patients will have an MRI of the affected shoulder within two weeks of the anticipated subacromial decompression. MRI interpretation will be in the form of a radiological report documenting the presence or absence of rotator cuff tears or tendonitis, glenohumeral labral pathology, or other pathology about the shoulder. Intraoperatively the surgeon will record his findings both before and after review of the MRI and the MRI report. However, he will remain blinded to the MRI results until a surgical course has been decided intraoperatively. In other words, the surgery will begin as if no MRI had been performed. After an operative diagnosis and treatment course planned, the MRI and its report will be reviewed. If indicated by the MRI, the planned treatment course will be altered intraoperatively. Any and all treatment alterations based on the MRI will be recorded, and correlations will be made between pathology on surgical observation and those seen on the MRI.

Using open acromioplasty as the gold standard, after 100 surgeries the data will be reviewed to determine the SN, SP, NPV, and PPV, and accuracy of MRI. The need for preoperative MRI will be assessed by determining whether and how many operative plans are affected by the MRI and its interpretation.

**Progress :** No patients yet enrolled due to modifications pending final approval by involved participants.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 86/016	<b>Status:</b> Terminated
<b>Title:</b> Teaching Program for Practical Microsurgery		
<b>Start Date:</b> 11/15/85	<b>Est. Completion Date:</b> Indef.	
<b>Department:</b> Surgery, Orthopedics Service	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Frederic L. Johnstone, MC		
<b>Associate Investigators:</b>		
COL Jackie L. Finney, MC	COL Richard A. Camp, MC	
LTC Donald B. Blakeslee, MC	COL Thomas G. Griffith, MC	
MAJ Stephen D. Clift, MC	LTC Robert J. Kenevan, MC	
LTC Bruce R. Wheeler, MC	MAJ Viswanatham Piratla, MC	
MAJ Michael Q. Cosio, MC	MAJ Michael R. Morris, MC	
	MAJ Stephen M. Davis, MC	
<b>Key Words:</b> training protocol, microsurgery, Animal Study		
<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$690.00	06/10/94

**Study Objective:** To perfect the techniques needed to perform clinical microsurgery and to establish formal training programs in clinical microsurgery at MAMC for use of those surgeons desiring to develop this expertise.

**Technical Approach:** A schedule of one or two afternoons per week will be set aside for teaching sessions. Sessions will begin with lectures, followed by practical exercises in anatomy and step-by-step instruction in the surgical techniques. Staff and residents from the Orthopedic, Plastic Surgery, and Thoracic Surgery Services will train in the following procedures: (1) reimplantation of extremities, (2) re-anastomosis of peripheral vessels and nerves, (3) repair of avulsion wounds, (4) graft transplants, (5) free cutaneous, myocutaneous and composite tissue transfer for traumatic lesions and reconstructive procedures, (6) re-anastomosis of facial nerve lesions. The training will begin with small vessels and nerves in cadaver specimens of small laboratory animals. When the anatomy of the area is learned as well as the use of the microsurgical instruments and the operating microscope, then microsurgical procedures in living rats, guinea pigs, and rabbits can be learned.

**Progress :** No programs were done in FY 95. Protocol was rewritten is now protocol number 95/012.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/102		<b>Status:</b> On-going	
<b>Title:</b> Teaching Program for Practical Microsurgery Using Rats As A Model					
<b>Start Date:</b> 03/24/95			<b>Est. Completion Date:</b> Mar 98		
<b>Department:</b> Surgery, Orthopedics Service			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Frederic L. Johnstone, MC					
<b>Associate Investigators:</b>			CPT Vernon S. Esplin, MC		
<b>Key Words:</b> Microsurgery:training, rat model,Animal Study					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//	

Study Objective: This teaching protocol will establish a formal training program in clinical microsurgery for orthopedic residents at MAMC. It will provide microsurgery practice in the repair of small vessels, nerves and tendons of the rat which model those of the hands, face and other body parts of humans.

Technical Approach: One rat will be used per week for 52 weeks for continuous microsurgery training for orthopedic residents. The rats will be placed under general anesthesia, used for numerous practice repairs and then humanely euthanized at the conclusion of the surgical procedures. Specifically, the femoral artery of the rat serves as an excellent model of small human vessels and will be repeatedly cut and repaired. Residents will be tested after six weeks by oral examination and should be capable of performing extremity revascularizations.

Progress : 4 rats were used in one program in FY 95.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/128		<b>Status:</b> On-going	
<b>Title:</b> Use of Pulsing Electromagnetic Fields to Potentiate Healing of Traumatic Combat and Training Injuries					
<b>Start Date:</b> 05/19/95			<b>Est. Completion Date:</b> Dec 97		
<b>Department:</b> Surgery, Orthopedics Service			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Delbert E. Casey Jones, MC					
<b>Associate Investigators:</b> MAJ Richard T. Dombroski, MC Estelle Hamblen, BA, MHA			LTC Richard A. Sherman, MS Antje F. W. Goeken, Psy.D. Melissa Wong, BA		
<b>Key Words:</b> Pulsing electromagnetic fields, injuries:combat, injuries:training					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		//	

**Study Objectives:** The overall objectives of the program are to determine whether pulsing electromagnetic fields (PEMFs) can be useful in potentiating recovery from combat wounds and training injuries when used in conjunction with standard techniques by (1) increasing the rate of healing while reducing swelling after hand, anterior cruciate ligament (ACL), and foot surgery or simple fractures of the long bones faster and further than standard techniques and (2) reduce the recovery time after stress fractures and ACL-related knee pain.

**Technical Approach:** This project is designed to determine whether exposure to PEMFs can potentiate healing of (a) traumatic combat and (b) training injuries including wounds, stress fractures, sprains, and ACL tears. These are representative of the types of injuries commonly seen in both combat and training. It is part of a program designed to prevent, track, and treat extremity trauma and training injuries among combat soldiers which should result in less loss of time away from the unit. It is the successor to the MRDC-funded project entitled "Use of body surface heat patterns for predicting and evaluating acute lower extremity pain among soldiers" (MRDC #8913004). We intend to study at least 40 subjects of each treatment/injury group. The major variables to be studied are (1) reduction of swelling and (2) increase in the rate of healing. The data will be analyzed separately for hand surgery, foot surgery, ACL repair, and long bone fractures with sub-types co-varied. The pre-surgical baseline measurements of swelling will be compared with daily measurements and the operated extremity will be compared with the intact extremity using a two way, repeated measures analysis of co-variance.

**Progress :** No subjects have been entered. We were recently informed that MAMC will not fund this study so it will be performed as time permits.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/160	<b>Status:</b> On-going
<b>Title:</b> Use of Pulsing Electromagnetic Fields for the Treatment of Pelvic Stress Fractures		
<b>Start Date:</b> 09/21/94	<b>Est. Completion Date:</b> Sep 95	
<b>Department:</b> Surgery, Orthopedics Service	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Delbert E. Casey Jones, MC		
<b>Associate Investigators:</b> LTC David J. Magelssen, MC Antje F. W. Goeken, Psy.D.		LTC Richard A. Sherman, MS A. Kungys
<b>Key Words:</b> Stress fractures:pelvic, electromagnetic fields		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** To determine whether application of Pulsing Electromagnetic Fields (PEMFs) over the stress fracture site, used in conjunction with standard therapeutic approaches, reduces the time to return to full duty in relation to those receiving the standard treatments and placebo PEMFs.

**Technical Approach:** Subjects diagnosed as having pelvic area stress fractures will receive one hour of PEMF or placebo PEMF therapy five days per week in addition to the standard treatment (sharply reduced activity and minimized walking) from the time the diagnosis is made until return to full duty. Subjects will be randomly assigned to groups and evaluated.

The patient will lay on an exam table with the head of the PEMF generator positioned several millimeters above the stress fracture site. The patient will be exposed to the fields for 15 minutes while on their backs and an additional 15 minutes while on their fronts. Each subject will have a total of 30 exposure to the field every day until they return to duty. The machine makes the same humming sound regardless of whether or not it is generating a field and subjects can not feel the field. Thus, subjects should not be aware of whether they are in the exposure or placebo group. The technician who turns on the device will know which group the subject is in so the machine can be set for either actual or placebo functioning but the technician and physicians doing the evaluations will have no idea which group the patients are in.

**Progress :** 8 subjects were entered this FY. Recruitment of subjects is continuing.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/155		<b>Status:</b> On-going	
<b>Title:</b> Establishment of the Natural History/Progression of Pediatric Fingernail Injury Outcomes					
<b>Start Date:</b> 07/21/95			<b>Est. Completion Date:</b> May 97		
<b>Department:</b> Surgery, Orthopedics Service			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Delbert E. Casey Jones, MC					
<b>Associate Investigators:</b> CPT George K. Bal, MC			CPT James T. Vandenberg, MC		
<b>Key Words:</b> Fingernails, pediatric, injuries, natural history					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> //

**Study Objective:** To establish the natural history of fingernail injury outcomes in children (1-8 years of age) with and without any distal phalanx fractures treated in the MAMC Emergency Department. To determine whether there is a need for follow-up studies on treatment procedures designed to reduce permanent abnormalities in the nails.

**Technical Approach:** Trauma is a major cause of pediatric fingernail injuries. In children, traumas may result in hematoma formation or nail avulsion. When the nail matrix and bed are unaffected, the effects are temporary. If the matrix or nail bed is injured, permanent scarring of the nail may result. Among adults, long term effects of trauma may include scarring and dystrophy of the nail if early treatment is not initiated.

Fifty children with fingernail injuries will be studied. Parents of the children meeting the entry criteria will be asked to participate. The child's injury will be assessed and photographed at the time of injury, and at followup visits at six week intervals for six months. A rate of abnormal healing will be determined and associated with cause and severity of the initial injury.

**Progress :** Six subjects have been entered. Recruitment of subjects will continue.



## Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 95/140

**Status:** On-going

**Title:** Randomized Prospective Treatment with Low Molecular Weight Heparin in Patients Treated with Plaster Immobilization of the Lower Extremities

**Start Date:** 05/19/95

**Est. Completion Date:**

**Department:** Surgery, Orthopedics Service

**Facility:** MAMC

**Principal Investigator:** MAJ John D. Pitcher Jr., MC

**Associate Investigators:**

CPT George K. Bal, MC  
CPT Christopher D. Cannon, MC  
CPT Randall K. Hildebrand, MC  
MAJ Arnoldas S. Kungys, MC  
CPT Joseph A. Shrout, MC

LTC David F. J. Tollefson, MC  
CPT Barry T. Bickley, MC  
L. Harriman  
CPT Michael E. Kirk, MC  
CPT Marc J. Michaud, MC  
CPT Mark C. Weston, MC

**Key Words:** DVT, casts, heparin

**Accumulative**

**MEDCASE Cost:** \$0.00

**Est. Accumulative**

**OMA Cost:** \$0.00

**Periodic Review:**

//

**Study Objectives:** To determine whether treatment with low molecular weight heparin in patients with short and long casts prevents or decreases the incidence of deep venous thrombosis (DDT). To determine the true incidence of DDT in patients treated with lower extremity immobilization for various age groups and risk factor assessment.

**Technical Approach:** Three hundred consecutive patients treated for orthopedic injuries or with orthopedic surgery who also require lower extremity immobilization will be randomized into groups of patients treated either with and without low molecular weight heparin. (This group of patients will be used to complete the first objective). Categories of patients will include operative and non-operative patients, short and long leg casts, and casts that are weight bearing and non-weight bearing. Prescription medications will be logged. Patients with a high risk for pulmonary embolism will be excluded from the study and treated in the standard fashion with coumadin. For all patients, post treatment sonographic evaluation will be obtained to document the incidence of DVT. Those patients not agreeing to randomization (the number of which ends when the first group's number reaches 300) will be enrolled at their consent to obtain post-casting sonography to aid in determining the incidence for DDT. (This group will be used to complete the second objective). Demographic data and associated medical illnesses will be recorded for all patients. The two groups (randomized patients and those refusing randomization) will be compared to determine if the groups are matched. The rate of thrombosis occurrence in each group will be initially compared using chi-square. A discriminate factor analysis will be used to determine whether any of these categories (or any combination) can predict occurrences of thrombosis.

**Progress :** No subjects have been entered, still trying to get funding.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/180		<b>Status:</b> On-going	
<b>Title:</b> Lateral Ankle Reconstruction Study					
<b>Start Date:</b> 09/02/94			<b>Est. Completion Date:</b> Apr 95		
<b>Department:</b> Surgery, Orthopedics Service			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT James D. Swenson, MC					
<b>Associate Investigators:</b> CPT Mark C. Weston, MC			MAJ John D. Pitcher Jr., MC		
<b>Key Words:</b> ankel reconstruction					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		//

**Study Objective:** Evaluate functional (subjective) and mechanical (objective) improvement in patients undergoing reconstruction of lateral ankle ligaments.

**Technical Approach:** Patients found to have unstable lateral ankle ligaments will undergo surgery to reconstruct these ligaments. They will be evaluated before surgery with radiographs and a physical examination of the ankle to determine the amount of pre-operative laxity. Patients will be followed after surgery for at least 6 months at which time repeat radiographs and physical examination of the ankle will be done to determine the amount of post-operative ankle laxity. Patients will also be asked to fill out a questionnaire regarding the functional status of their ankle.

**Progress :** Over the last year initial data has been compiled on all 30 patients. Have begun seeing patients for their 6 month followup. Plan to see all patients for their followup by June 1996.

## Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 95/174

**Status:** On-going

**Title:** Comparative Effectiveness of (a) Standard Treatment, (b) Standard Treatment Plus Force Measured Orthotic Cutting Methodologies, (c) Standard Treatment Plus Pulsing Electromagnetic Fields, and (d) A ..

**Start Date:** 07/21/95

**Est. Completion Date:**

**Department:** Surgery, Orthopedics Service

**Facility:** MAMC

**Principal Investigator:** K. Willard

**Associate Investigators:**

LTC Richard A. Sherman, MS

P. Block

Kimberly A. Hermann-Do, BS, MHA

Melissa Wong, BA

S. Wilkerson

J. Gonzales

Estelle Hamblen, BA, MHA

Linda Robson, BA

**Key Words:** Ulcers:lower limbs, ulcers:feet, pulsed electromagnetic fields

**Accumulative**

**MEDCASE Cost:** \$0.00

**Est. Accumulative**

**OMA Cost:** \$0.00

**Periodic Review:**

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**Study Objectives:** To compare the effectiveness of (a) standard treatment plus placebo pulsing electromagnetic fields (PEMFs), (b) standard treatment plus force measured orthotic cutting methodologies, (c) standard treatment plus PEMFs, and (d) a combination of all three for treatment of stable, open ulcers on the lower limbs and feet.

**Technical Approach:** We propose to perform a double-blinded study utilizing metabolically abnormal patients (mostly diabetic) with skin ulcers on their feet and lower legs which have not healed during the previous three months. Participants will be stratified by age, grade of ulcer, diameter of ulcer, and location of ulcer. Patients will then be randomized to one of the four groups described above. During the initial evaluation, all patients will be evaluated for pressure/force patterns and for blood flow to the ulcer. All patients, except those in the orthotics only group, will receive real or placebo PEMF therapy for five days per week for one hour per day until the ulcer heals or six weeks of treatment. Rate of ulcer healing will be measured by photography and videothermogram. Foot pressure patterns produced while standing still and walking will be measured at each evaluation session using automated pressure sensors set to average the pressure at each square cm of the sole. A power analysis of the pilot results shows that 33 subjects will be needed in each group assuming that we predict the PEMF/orthotic group will do better (one-tailed test) and an 80% chance of finding a difference between the four groups at a 0.05 level of significance. A total of 150 subjects will have to be started to account for dropouts. The data will be analyzed using a repeated measures analysis of variance.

**Progress :** Study has not started, awaiting funding.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF SURGERY, PLASTIC SURGERY**  
**SERVICE**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 92/099		<b>Status:</b> Terminated	
<b>Title:</b> The Implantation of Bone Morphogenic Protein Using Vascularized Omentum in a Predetermined Size and Shape in Swine					
<b>Start Date:</b> 09/04/92			<b>Est. Completion Date:</b> Dec 92		
<b>Department:</b> Surgery, Plastic Surgery Svc			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Stephen M. Davis, MC					
<b>Associate Investigators:</b> MAJ Robert J. Wygonski, DC			MAJ Cecil R. Dorsett, DC MAJ Richard R. Gomez, MC		
<b>Key Words:</b> bone protein, omentum, animal study,Animal Study					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$600.00		06/07/93	

**Study Objective:** To determine if a vascularized graft utilizing omentum with bone morphogenetic protein can induce bone formation in a three dimensional shape; and to determine bone produced in this manner can survive transplantation to a different location.

**Technical Approach:** Bone grafting is a commonly performed procedure. The best bone graft is a vascular autogenous graft (one obtained from the patient complete with its own blood supply). However, this is not always possible and does have certain risks, even when properly performed. Bone morphogenetic protein (BMP) is a substance which induces new bone to form in intra- or extra-skeletal sites and has recently been cloned by recombinant DNA techniques. Six pigs will be used for this study. Each pig will undergo a laparotomy with the placement of six tubular molds around individual omental pedicles. Two molds will contain only omentum, two will contain omentum and autogenous bone, and two will contain omentum and bone morphogenetic protein. Forty five days after being implanted, each mold will be opened and visually examined. The two molds containing bone morphogenetic protein will have their vascular supply switched by microsurgical techniques. After an additional 45 days, all molds will be harvested and examined to determine if bone has been produced in a three dimensional shape with its own blood supply. If present, an attempt will be made to determine if it is cortical, cancellous, or corticocancellous bone.

**Progress :** Initial work did produce bone within omentum, however lack of time by the PI to complete the project.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF SURGERY, UROLOGY SERVICE**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/144		<b>Status:</b> On-going	
<b>Title:</b> Evaluation of the Safety and Efficacy of Transurethral Resection of the Prostate Using the Contatct Laser System vs Electrosurgery					
<b>Start Date:</b> 09/02/94			<b>Est. Completion Date:</b>		
<b>Department:</b> Surgery, Urology Service			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Kurt L. Hansberry, MC					
<b>Associate Investigators:</b> MAJ J. Brantley Thrasher, MC			COL John N. Wettlaufer, MC		
<b>Key Words:</b> prostate:resection, laser, electrosurgery					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//	

**Study Objective:** 1. To evaluate the effectiveness (resection and coagulation) of the Contact Laser System in comparison to that of electrosurgery for transurethral resection of the prostate (TURP).

2. To evaluate the relative cost effectiveness of the Contact Laser in comparison to that of electrosurgery for transurethral resection of the prostate.

**Technical Approach:** Male patients who have been diagnosed with symptomatic benign prostatic hypertrophy (BPH) will be enrolled into this study once all of the entrance criteria have been fulfilled. After all baseline evaluations have been performed, each patient will undergo TURP using either electrosurgery or the Contact Laser System. All patients will be monitored closely through discharge, and will undergo follow-up evaluation at one and six months, and one year following surgery. Follow-up evaluation will be encouraged (optional) annually for five (5) years thereafter.

**Progress :** 14 subjects have been enrolled. Enrollment is slower than expected. The majority of patients are experiencing subjective and objective improvement in their voiding patterns.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/104		<b>Status:</b> On-going	
<b>Title:</b> Telomere Length and Telomerase Activity in Human Testicular Cancer					
<b>Start Date:</b> 06/16/95			<b>Est. Completion Date:</b> Jul 97		
<b>Department:</b> Surgery, Urology Service			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Raymond S. Lance, MC					
<b>Associate Investigators:</b>			CPT Wade K. Aldous, MS		
MAJ J. Brantley Thrasher, MC			MAJ Kenneth W. Westphal, MC		
K.J. O'Reilly			Troy H. Patience, B.S.		
<b>Key Words:</b> Cancer:testicular, telomerase					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		//	

**Study Objectives:** This study encompasses four objectives. To determine the presence or absence of telomerase activity in tumorous testicular tissue and normal tissue. To observe the average telomeric length of both tissue types to compare differences in length, hypothesizing that tumor tissue would have shorter telomeres. To quantify telomerase activity in tissues with an active enzyme. To determine the relationship, if any, between activity of telomerase and the stage and grade of testicular cancer.

**Technical Approach:** Tissue samples will be taken from 40 male patients undergoing surgical resection for testicular cancer. All malignant and benign tumor types resected during surgery will be investigated. Tissue from the tumor and from surrounding histologically normal areas will be transferred from the Dept. of Pathology to the Dept. of Clinical Investigation. Genomic DNA will be extracted from the tissues and subjected to *Rsa*I and *Hinf*I restriction digestion. The fragments will then be separated by agarose gel electrophoresis, Southern blotted, and detected by chemiluminescence using a digoxigenin-labeled telomere probe. These will be visualized by x-ray film exposure and will provide the composite lengths of all telomeres in a cell population. Actual telomerase activity in tumorous and normal tissue will also be measured by extracting the enzyme from tissues and assaying for activity. The positive control is an immortalized cell line. Activity is measured by the successful incorporation of radio-labeled dGTP nucleotide into the telomere repeats on a known DNA primer. These will be separated on a polyacrylamide gel and quantified by densitography. The differences in telomere length will be tested by a non-parametric T-test. Chi-square analysis will be used to test for telomerase activity assuming normal tissue has inactive enzyme and tumor tissue has active enzyme. The paired T-test will be used to quantify telomerase activity compared to positive controls and a non-parametric ANOVA will be used to determine the correlation between the amount of activity and the stages and grades of tumors.

**Progress :** 5 tumors have been analyzed after development of the assay was satisfactory. We have concluded that telomere length provides no important information in testis and colon tumors. Study will continue and look at other types of tumors.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/109		<b>Status:</b> On-going	
<b>Title:</b> Telomere Length and Telomerase Activity in Human Transitional Cell Carcinoma					
<b>Start Date:</b> 04/21/95			<b>Est. Completion Date:</b> Jul 97		
<b>Department:</b> Surgery, Urology Service			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Raymond S. Lance, MC					
<b>Associate Investigators:</b> CPT Wade K. Aldous, MS			MAJ J. Brantley Thrasher, MC Troy H. Patience, B.S.		
<b>Key Words:</b> Cancer: bladder, telomere, temomerase					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		//	

**Study Objective:** This study encompasses four objectives. To determine the presence or absence of telomerase activity in transitional cell carcinoma tissue and normal tissue. To observe the average telomeric length of both tissue types to compare differences in length, hypothesizing that tumor tissue would have shorter telomeres. To quantify telomerase activity in tissues with an active enzyme. To determine the relationship, if any, between activity of telomerase and the stage and grade of human transitional cell carcinoma.

**Technical Approach:** Tissue samples will be taken from 40 male and female patients undergoing operative resection for bladder cancer. All malignant and benign tumors of the bladder found during surgery will be investigated. Tissue from the tumor and from surrounding histologically normal areas will be transferred from the Dept. of Pathology to the Dept. of Clinical Investigation. Genomic DNA will be extracted from the tissues and subjected to *Rsa*I and *Hinf*I restriction digestion. The fragments will then be separated by agarose gel electrophoresis, Southern blotted, and detected by chemiluminescence using a digoxigenin-labeled telomere probe. These will be visualized by x-ray film exposure and will provide the composite lengths of all telomeres in a cell population. Actual telomerase activity in tumorous and normal tissue will also be measured by extracting the enzyme from tissues and assaying for activity in vitro. The positive control is an immortalized cell line. Activity is measured by the successful incorporation of radio-labeled dGTP nucleotide into telomere repeats on a known DNA primer. The modified primers will be separated on a polyacrylamide gel and quantified by densitography. The differences in telomere length will be tested by a non-parametric T-test. Chi-square analysis will be used to test for telomerase activity assuming normal tissue has inactive enzyme and tumor tissue has active enzyme. The paired T-test will be used to quantify telomerase activity compared to positive controls and a non-parametric ANOVA will be used to determine the correlation between the amount of activity and the stages and grades of tumors.

**Progress :** 7 tumors have been analyzed after development of the assay was satisfactory. We have concluded that telomere length provides no important information in testis and colon tumors. Study will continue and look at other types of tumors.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/132		<b>Status:</b> Completed	
<b>Title:</b> Fluoroquinolones As Prophylaxis in Penile Prosthesis Surgery					
<b>Start Date:</b> 07/02/93			<b>Est. Completion Date:</b> Jun 96		
<b>Department:</b> Surgery, Urology Service			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Bradley F. Schwartz, MC					
<b>Associate Investigators:</b> MAJ Kurt L. Hansberry, MC			MAJ J. Brantley Thrasher, MC		
<b>Key Words:</b> penile prosthesis, fluoroguinolones, prophylaxis					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		10/21/94	

**Study Objective:** To determine if oral Fluoroquinolones afford efficacious alternatives to the current regimens in penile prosthetic surgery prophylaxis.

**Technical Approach:** All patients undergoing elective penile prosthesis surgery at Madigan Army Medical Center will be given one of the following preoperative antibiotic prophylaxis regimens: Fluoroquinolone two hours prior to surgery, the evening of surgery and for seven days following surgery; or a combination of gentamycin 75 mg and Cefazoline 1 gm two hours preoperatively and cephradine 250 mg qid for seven days postoperatively. Intraoperatively, a 1 cm<sup>3</sup> sample of the corpus cavernosum will be taken and sent to the University of Washington Department of Pathology for quantitative tissue determinations of the antibiotic using a bioassay. At the same time, a determination of serum concentration of the drug will be made.

**Progress :** 20 subjects have been entered. There is a statistical difference in favor of ofloxacin vs peternal ABX in the prophylaxis of penile prosthesis surgery. There is also a significant cost savings using the oral regimen thus eliminating an overnight hospital stay.

### Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 94/133

**Status:** On-going

**Title:** Comparison of Self-Injection versus External Vacuum Devices in the Treatment of Erectile Dysfunction

**Start Date:** 08/05/94

**Est. Completion Date:**

**Department:** Surgery, Urology Service

**Facility:** MAMC

**Principal Investigator:** CPT Douglas W. Soderdahl, MC

**Associate Investigators:**  
MAJ Kurt L. Hansberry, MC

MAJ J. Brantley Thrasher, MC

**Key Words:** erectile dysfunction, self-injection devise, external vacuum devise

**Accumulative**

**Est. Accumulative**

**Periodic Review:**

**MEDCASE Cost:** \$0.00

**OMA Cost:** \$0.00

//

**Study Objective:** To directly compare two non-surgical treatments of erectile dysfunction: self-injection vs. external vacuum devices.

**Technical Approach:** Patients actively undergoing either self-injection pharmacotherapy or external vacuum device (EVD) therapy will be invited to participate in this study. Each patient enrolled will receive a detailed questionnaire which covers satisfaction, effectiveness, and side effect issues of their currently employed treatment modality. The self-injection group will then be given instruction and necessary equipment to employ the EVD. Likewise, the EVD group will receive instructions for injection treatment. After four months, the participants will be asked to complete the same questionnaire to evaluate the alternate modality. The participants will also be asked to comment on their comparison of the two therapies. Sexual partners of the patients will also be asked to attend a follow-up visit and fill out a confidential questionnaire comparing the two different treatments. At the end of the study, the patient and his physician will make an informed decision about which modality to continue with.

**Progress :** 50 patients have entered study, with complete data on 44. Both the EVD and ICSI regimens are effective treatment modalities for impotence. While ICSI shows a statistically significant advantage over EVD in patient and partner satisfaction, the clinical significance of this is unclear. The subjective observations from the participants may aid the urologist in making informed recommendations concerning these therapies.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/173		<b>Status:</b> On-going	
<b>Title:</b> The Role of Urine Cytology in the Surveillance of Bladder Cancer					
<b>Start Date:</b> 09/15/95			<b>Est. Completion Date:</b> Jun 96		
<b>Department:</b> Surgery, Urology Service			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Douglas W. Soderdahl, MC					
<b>Associate Investigators:</b> MAJ Kurt L. Hansberry, MC			MAJ J. Brantley Thrasher, MC		
<b>Key Words:</b> Cancer:bladder, urine cytology					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//	

Study Objectives: To determine the role of urine cytology in the surveillance of bladder cancer.

Technical Approach: The purpose of this study is to determine how urine cytologies can be used in the diagnosis and follow-up of bladder cancer. There are two questions we are trying to answer. We would like to know if urinary cytology has sufficient sensitivity and specificity to potentially eliminate the need for bladder mapping or at least reduce the number of indications for which this is utilized. In addition, we would like to know if urine cytologies might be used confidently in the follow-up of bladder cancer so that the number of surveillance cystoscopies might be reduced. We will involve up to 100 patients with known bladder cancer and those who present with signs and symptoms consistent with bladder cancer. All patients with a positive cytology and/or suspicious visible lesions will undergo random bladder biopsies with or without transurethral resection of bladder tumor. Biopsy results will be used as the gold standard. Bladder barbotage (washing) samples will be obtained by instilling and withdrawing approximately 50cc of normal saline repeatedly to obtain a fresh sample. This cytology sample will be evaluated promptly, since the handling of these samples has been shown to affect the sensitivity of the cytology. We want to then compare these results to that of the biopsy. The sensitivity, specificity, predictive value and negative predictive value will be determined.

Progress : Still in process of data collection with 30 subjects currently entered.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/134		<b>Status:</b> On-going
<b>Title:</b> Comparative Study of the Clinical Efficacy of Two Dosing Regimens of Eulexin[colon] 250 mg Q8h vs 500 mg QD				
<b>Start Date:</b> 05/19/95			<b>Est. Completion Date:</b> Jul 96	
<b>Department:</b> Surgery, Urology Service			<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ J. Brantley Thrasher, MC				
<b>Associate Investigators:</b> COL John N. Wettlaufer, MC			MAJ Kurt L. Hansberry, MC	
<b>Key Words:</b> Cancer:prostate, Eulexin				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>	
\$0.00		\$0.00	//	

**Study Objectives:** To compare the clinical effectiveness of a new dosing regimen (500mg QD) for administering flutamide to the currently indicated dosing regimen of 250 mg Q8H according to (1) the percent of patients normalizing PSA and (2) quality of life differences between the two regimens.

**Technical Approach:** This phase IV, multi-center, open label, prospective randomization study will include 400 patients (10 from MAMC), ages 40 to 85, with clinically proven and histologically confirmed adenocarcinoma of the prostate gland. The subjects will be randomized to one of two treatment groups, Flutamide 250mg Q8H or Flutimade 500 mg QD, at Time 0. Time 0 is the day of surgical or medical castration. The study treatments will be continued for three months. The two variables to be evaluated are normalized PSA values as determined by standard laboratory PSA test, and quality of life as determined by questionnaire. Laboratory tests will be taken at clinic visits at Time 0, and weeks 4, 8, and 12. PSA normalization will be performed on 12 weeks data after the last patient accrued has reached the 12 week point. In order to achieve the conventional 80% power for showing equivalence, 200 patients per arm will be required based on a threshold criterion of 15%. Evaluation of the Quality of Life modules will involve multivariate analysis of variance for repeated measures for HQL domains and symptoms. Treatment by time interaction effect will be assessed under the repeated measures model to identify HQL domains that are significantly different between the two treatment arms using a two-sided 5% level test.

**Progress :** This study has just begun with 3 subjects currently entered. Elevated LFT's on one patient. Resolved when study drug withdrawn. No complications.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/164		<b>Status:</b> On-going
<b>Title:</b> Prostate Cancer Intervention vs Observation Trial (PIVOT)[colon] A Randomized Trial Comparing Radical Prostatectomy vs Palliative Expectant Management for the Treatment of Clinically Localized Prostate ...				
<b>Start Date:</b> 09/21/94		<b>Est. Completion Date:</b> Sep 04		
<b>Department:</b> Surgery, Urology Service		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ J. Brantley Thrasher, MC				
<b>Associate Investigators:</b>		MAJ Kurt L. Hansberry, MC		
<b>Key Words:</b> Cancer:prostate, prostatectomy, palliative management				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//

**Study Objective:** To determine which of 2 treatment strategies is superior in reducing all-cause mortality in patients with clinically localized prostate cancer (1) radical prostatectomy and early intervention of subsequent disease persistence or recurrence or (2) expectant management with reservation of therapy for palliative treatment of symptomatic or metastatic disease progression.

**Technical Approach:** Patients will be randomized to one of the two groups listed (1) will have a radical prostatectomy; (2) will be assigned to Watchful Waiting Management.

Patients in group 1 will have 2 surgical procedures; removal of the lymph nodes from near the prostate gland (pelvic lymph node surgery); and then proceed with the prostatectomy.

Patients in group 2 will not have their cancer removed. Patients will be closely observed; if the cancer causes symptoms, treatment will be aimed at providing relief of these symptoms.

**Progress :** No patients have yet met inclusion criteria.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/083	<b>Status:</b> On-going
<b>Title:</b> Diet and Prostate Hormones		
<b>Start Date:</b> 03/17/95	<b>Est. Completion Date:</b> Jul 95	
<b>Department:</b> Surgery, Urology Service	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ J. Brantley Thrasher, MC		
<b>Associate Investigators:</b> Stephen R. Plymate, M.D.		Alan R. Kristal, Dr.P.H. Johanna Lampe, Ph.D.
<b>Key Words:</b> Cancer:prostate, diet, prevention		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** 1) To better understand the relationships of diet with prostate cancer.  
2) To evaluate the potential value of dietary change for the primary prevention or adjuvant therapy of prostate cancer.

**Technical Approach:** This study will recruit 10 men with newly-diagnosed, localized and histologically well-differentiated prostate cancer who elect to undergo prostatectomy. They will be randomized into two arms: 1) low fat (20%en) and high fruit and vegetable (8+ servings/day) diet for 4-6 weeks before prostatectomy or 2) their usual diet. Dihydrotestosterone and Testosterone concentrations will be measured in blood, prostate biopsies, and prostate tissue removed at prostatectomy.

**Progress :** This study has just begun with 2 subjects currently entered.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/150		<b>Status:</b> On-going	
<b>Title:</b> Center for Prostate Disease Research Prostate Cancer Radical Prostatectomy Follow-up Questionnaire					
<b>Start Date:</b> 06/16/95			<b>Est. Completion Date:</b> Sep 95		
<b>Department:</b> Surgery, Urology Service			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ J. Brantley Thrasher, MC					
<b>Associate Investigators:</b>			J.W. Moul		
<b>Key Words:</b> Cancer:prostate, prostatectomy, questionnaire					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> //

**Study Objective:** The objective of this study is to conduct a comprehensive survey of men who have undergone a radical prostatectomy (RP) for prostate cancer (PC) to assess long-term quality of life (QOL) regarding impotence, incontinence and surgical complications.

**Technical Approach:** In 1994 there have been over 200,000 new cases of PC diagnosed in the United States, and the use of RP as a treatment modality has increased over 200% since the mid 1980's. With the increasing use of RP, more attention has focused on side effects and complications of the treatment and how they relate to overall QOL in these men. In a multicenter study (WRAMC and MAMC), a QOL questionnaire, regarding impotence, incontinence and surgical complications has been developed. This questionnaire will be mailed to subjects recruited from the database of all RP patients treated at MAMC and WRAMC between 1980-1994. A total of 400 returned questionnaires will be sufficient for data analysis. Most of the results will be descriptive statistics of morbidity percentages. Logistic regression will be used to model long-term quality of life outcome variables.

**Progress :** 554 subjects having undergone radical prostatectomy have been entered. Incontinence was reported in 38.4% of patients. Impotence was reported in 88% of the patients. More data analysis is planned.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/051		<b>Status:</b> On-going	
<b>Title:</b> Immunohistochemical Localization of Insulin-Like Growth Factor (IGF) Binding Proteins in Prostate Cancer					
<b>Start Date:</b> 04/01/94			<b>Est. Completion Date:</b> Jan 95		
<b>Department:</b> Surgery, Urology Service			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ J. Brantley Thrasher, MC					
<b>Associate Investigators:</b> MAJ Richard R. Gomez, MC CPT Patrick A. Twomey, MC			Stephen R. Plymate, M.D. CPT Michael D. Bagg, MC		
<b>Key Words:</b> cancer:prostate, IGF					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> //

**Study Objective:** The purpose of this study is to localize IGFBP's -2,-3,-4, and -6 in regions of histologically proven prostate cancer. Additionally, these same techniques will be used to identify these binding proteins in areas of prostatic intraepithelial neoplasia (PIN) and benign prostatic hyperplasia (BPH). The information gleaned from this study will help better understand IGFBP expression in both malignant, premalignant, and benign prostatic tissue.

**Technical Approach:** Radical prostatectomy specimens will be obtained by the Urology Service and taken to Pathology for histologic sectioning. Prostate adenocarcinoma will be identified in sections (as well as areas of PIN or BPH) with an adjacent section taken for immunohistochemical staining. Immunohistochemical staining will be performed for identification of IGFBP's -4, -2, -3, and -6 in regions of associated neoplasm, PIN or BPH. Approximately 10 patients will be studied with comparisons to be made between neoplastic premalignant, and benign prostatic tissue.

**Progress :** During this FY subject accrual has doubled from 20 to 40 patients. Future research will be directed toward the obvious clinical correlate which is attempting to block the growth factor binding proteins and the growth factors themselves to stop prostate epithelium growth.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF SURGERY, VASCULAR SURGERY**  
**SERVICE**

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/165		<b>Status:</b> On-going	
<b>Title:</b> A Double-Blind, Pharmacokinetic Comparative Study of Two Concentrations[colon] 1% and 3% Bucladesine Sodium Ointment (DT-5621) in Patients with Venous Stasis Ulcers					
<b>Start Date:</b> 07/21/95			<b>Est. Completion Date:</b> Sep 96		
<b>Department:</b> Surgery,Vascular Surgery Svc			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL Charles A. Andersen, MC					
<b>Associate Investigators:</b>			Edmund Kanar		
<b>Key Words:</b> Ulcer, bucladesine sodium					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> //

**Study Objective:** The primary objectives of this study are to determine the extent of potential systemic absorption of 1% and 3% bucladesine sodium ointments (DT-5621) following topical administration, by measuring plasma concentrations of the drug, and to determine the safety of topical 1% and 3% bucladesine sodium ointments (DT-5621) in patients with venous stasis ulcers of the lower limbs. The secondary objectives are to evaluate the efficacy endpoint for the Target Study Ulcer, to evaluate resource use data leading to pharmacoeconomic analysis and modeling, and to evaluate Quality Of Life data.

**Technical Approach:** This study is designed as a double-blind, randomized trial of 1% and 3% bucladesine sodium Ointments (DT-5621) in patients with venous stasis ulcers. This is a multicenter study that will enroll a total of approximately 80 patients, resulting in approximately 60 evaluable patients. A total of 6 patients will be enrolled at Madigan. Drug will be administered on an outpatient basis. During PK serial drawing days; Day one Week 2, and Day 1 Week 3, patient will stay at the study site for the duration of the blood draws and EKG recordings. Single samples are also drawn for PK (no EKGs) on Day one Week 6, Day one Week 10, and Day one Week 14. The study will be conducted in patients 18 to 85 years of age who are diagnosed as having venous stasis ulcer(s), of the lower limbs; patients with venous stasis ulcer(s) refractory to treatment, may also enter the study. Patients with lesion(s) ranging in size from 2 cm<sup>2</sup> up to 50 cm<sup>2</sup> will be eligible for the study. Each patient will be evaluated for 25 weeks, consisting of a 1-week Run-In Phase, followed by a 12 week Double-Blind Treatment Phase, and finally a 12 week Follow-Up Phase. Each investigator will try to enroll two patients in each of three ulcer size groups; patient with small ulcer(s), (2 cm<sup>2</sup> to 15 cm<sup>2</sup>), medium size ulcer(s), (16 cm<sup>2</sup> -35 cm<sup>2</sup>) and large ulcer(s), 36 cm<sup>2</sup>-50 cm<sup>2</sup>). Patients with up to three ulcers with (combined) surface area of 4 cm<sup>2</sup> (for 2 ulcers) or 6 cm<sup>2</sup> (for 3 ulcers) to 50 cm<sup>2</sup> may be entered into the study. However, each ulcer must be at least 2 cm<sup>2</sup>. Quality of life and size of the ulcer will be evaluated during the study.

**Progress :** Study has not been started yet, awaiting delivery of study drug.

### Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 94/174

**Status:** Terminated

**Title:** Assessing Quality of Life of Patients With Lower Extremity Arterial Occlusive Disease

**Start Date:** 09/02/94

**Est. Completion Date:**

**Department:** Surgery, Vascular Surgery  
Svc

**Facility:** MAMC

**Principal Investigator:** LTC Jon Charles Bowersox, MC

**Associate Investigators:** None

**Key Words:** Quality of Life: lower extremity arterial occlusive disease

Accumulative	Est. Accumulative	Periodic Review:
MEDCASE Cost: \$0.00	OMA Cost: \$0.00	//

**Study Objective:** The goal of this study is to use a questionnaire to longitudinally assess the health related quality of life in patients with lower extremity arterial occlusive disease.

**Technical Approach:** Patients will be required to fill out a questionnaire titled "Assessing Quality of Life of Patients with Leg Circulatory Problems" upon initial enrollment, one week later, 6 months, 12 months, 18 months and 24 months.

Physicians will complete the questionnaires titled "Physician's Expectations of Patient Outcomes" and "Longitudinal Patient Data Form" during initial enrollment of the patient. Physicians will complete the "Physician's Expectations" questionnaire again at 6 months, 12 months, 18 months, and 24 months.

The Principal Investigator will complete the "Comorbidity Score Sheet" after reviewing the patient's chart following initial enrollment and then the "Longitudinal Patient Data Form". The Principal Investigator will also complete "Comorbidity Score Sheet" and "longitudinal Patient Data Form" at the 6 month, 12 month, 18 month and 24 month intervals.

After completion, coded forms will be sent to the study coordinator center in White River Junction, VT.

**Progress :** 5 subjects were entered. PI retired and no other PI could be found. Since it was such a small accrual, no data analysis will be done.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/001	<b>Status:</b> Terminated
<b>Title:</b> A Double-Blind, Placebo-Controlled, Parallel Group, Randomized Study to Evaluate the Safety and Efficacy of Trental Oros ER Tablets in Patients With Intermittent Claudication		
<b>Start Date:</b> 10/21/94	<b>Est. Completion Date:</b> Oct 95	
<b>Department:</b> Surgery,Vascular Surgery Svc	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Jon Charles Bowersox, MC		
<b>Associate Investigators:</b> LTC David F. J. Tollefson, MC		COL Charles A. Andersen, MC Colleen Reimer
<b>Key Words:</b> claudication, Trental Oros ER Tablets		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objective:** The objective of this study is to determine whether Trental OROS prolongs Initial Claudication Distance (ICD) and Absolute Claudication Distance (ACD) in patients with intermittent claudication secondary to chronic arterial disease.

**Technical Approach:** The tablet Trental will be given to three groups of patients at different doses, plus a group receiving placebo. A complete medical history and physical exam will be done. Patients passing screening will receive a package of medication and instructions and asked to return to the study center once a week for four to six weeks, then once a month for six additional months. On each of these visits, patients will receive a new package of medication with instructions. The primary efficacy evaluation will be based on the walking distance to initial claudication (ICD) and to absolute (ACD).

**Progress :** This study was terminated by the sponsor. No subjects were enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/168	<b>Status:</b> Terminated
<b>Title:</b> Efficacy of an Oxygen Delivery Solution in Preventing Tissue Ischemia During Hypotensive Resuscitation From Hemorrhagic Shock in Guinea Pigs		
<b>Start Date:</b> 09/21/94	<b>Est. Completion Date:</b> Jun 95	
<b>Department:</b> Surgery,Vascular Surgery Svc	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Jon Charles Bowersox, MC		
<b>Associate Investigators:</b> R.L.S. Cornum CPT Stefan M. Pettine, MC		
<b>Key Words:</b> Ischemia, hemorrhagic shock, resuscitation, guinea pig,Animal Study		
<b>Accumulative</b> <b>MEDCASE Cost:</b>	<b>Est. Accumulative</b> <b>OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objective:** The objective of the proposed research is to determine if an oxygen delivery solution can prevent tissue ischemia during hypotensive resuscitation from hemorrhagic shock.

**Technical Approach:** The investigator will simulate hemorrhagic shock in anesthetized guinea pigs (*cavia porcellue*) by removing blood and maintaining the mean arterial blood pressure at 35 mm Hg. Animals will receive HBOC-201, a polymerized solution of bovine hemoglobin, and tissue oxygen levels will be measured. Control animals will receive either standard electrolyte solutions, hypertonic saline solutions or blood. At the end of the experiment, the anesthetized animals will be euthanized.

**Progress :** This protocol was terminated due to lack of funding.

**DETAIL SHEETS FOR PROTOCOLS**

**GYNECOLOGY ONCOLOGY GROUP**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 82/073		<b>Status:</b> On-going	
<b>Title:</b> GOG 0026A: Master Protocol for Phase II Drug Studies in Treatment of Advanced Recurrent Pelvic Malignancies					
<b>Start Date:</b> 11/20/81			<b>Est. Completion Date:</b> Indef.		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> COL William L. Benson, MC			COL Roger B. Lee, MC		
<b>Key Words:</b> malignancy:pelvic					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		02/05/93	

**Study Objective:** To implement a master protocol to screen for activity and efficacy of new agents or combinations in patients with advanced or recurrent pelvic malignancies, resistant to higher priority methods of treatment.

**Technical Approach:** A "rejection" type design will be used with a fixed sample size of 25 eligible patients/disease site/drug or combination studied. The design allows replacement of ineffective regimens by newer agents or combinations. Sections relating to specific agents will be sequentially incorporated into this protocol as these agents are studied. Continuing review will be done for each separate protocol. To be eligible, patients must have histologically confirmed, advanced, recurrent, persistent, metastatic, or local gynecologic cancer with documented disease progression; lesions that are measurable and can be followed for tumor response; abdominal, pelvic, or other masses which can be defined in at least two dimensions by palpation or by x-ray; a GOG performance Grade 0, 1, or 2 (Karnofsky scale 30-100); free of clinically significant infection; off previous chemotherapy for at least 3 weeks; recovered from effects of recent surgery, radiotherapy, or chemotherapy; passed the nadir blood counts from previous therapy and a granulocyte count  $>1500/\text{mm}^3$ , platelet count  $>100,000/\text{mm}^3$ , BUN  $<25 \text{ mg\%}$ , creatinine  $<1.5 \text{ mg\%}$ , bilirubin  $<1.1 \text{ mg}$ , SGOT  $<5 \text{ IU}$ . Patients receiving myelosuppressive agents will have adequate bone marrow function as described above. Exception to the general requirement for normal liver function will be secondary to documented metastatic tumor to the liver or as noted in the section dealing with that particular agent. Patients with all primary disease sites of gynecologic malignancies are eligible. Each disease site will be accumulated as a separate study sample. For a particular drug study, the allowable disease site(s) may be further qualified. Ascites and pleural effusion alone are not considered measurable for purposes of the study. A steady rise in the titers of alpha-fetoprotein and beta-HCG will be taken as evidence of disease progression in germ cell tumors of the ovary.

**Progress :** No new patients entered in FY 95.



### Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 82/007

**Status:** On-going

**Title:** GOG 0026C: A Phase II Trial of Cis-Platinum Diamminedichloride in Treatment of Advanced Pelvic Malignancies

**Start Date:** 11/20/81

**Est. Completion Date:** Indef.

**Department:** GOG

**Facility:** MAMC

**Principal Investigator:** LTC Mark E. Potter, MC

**Associate Investigators:**  
COL William L. Benson, MC

COL Roger B. Lee, MC

**Key Words:** cancer:pelvic,cisplatinum

**Accumulative**

**Est. Accumulative**

**Periodic Review:**

**MEDCASE Cost:** \$0.00

**OMA Cost:** \$0.00

02/05/93

**Study Objective:** To determine the efficacy of cis-platinum diamminedichloride in patients whose advanced malignancies have been resistant to higher priority methods of treatment.

**Technical Approach:** All patients with measurable gynecological cancer, who have failed higher priority therapies, will be offered cis-platinum as a Phase II drug to determine its efficacy. The drug is given at 50 mg/m<sup>2</sup> intravenously every three weeks as toxicity permits. Patients who respond or who demonstrate disease will continue to receive the agent until progression has occurred.

**Progress :** No new patients entered in FY 95.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 88/067		<b>Status:</b> On-going
<b>Title:</b> GOG 0026DD: A Phase II Trial of Amonafide (NSC #308847) in Patients with Advanced Pelvic Malignancies				
<b>Start Date:</b> 08/19/88		<b>Est. Completion Date:</b> Indef.		
<b>Department:</b> GOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> cancer:pelvic,amonafide				
<b>Accumulative MEDCASE Cost:</b> \$0.00		<b>Est. Accumulative OMA Cost:</b> \$0.00		<b>Periodic Review:</b> 02/05/93

**Study Objective:** To screen for activity of new agents or drug combinations in patients with advanced malignancies. Its intent is to determine the efficacy of chemotherapeutic agents in patients whose advanced malignancies have been resistant to high priority methods of treatment.

**Technical Approach:** Patients must have normal renal and hepatic function. Patients will be entered as non-randomized cases. Amonafide will be administered as a slow intravenous infusion over an hour at an initial dose of 300 mg/m<sup>2</sup> daily for five days. A serial dose escalation up to 450 mg/m<sup>2</sup> will be used in patient without toxicity after each cycle of therapy until a Grade 1 hematologic toxicity occurs. All patients will receive therapy until disease progression or until adverse effects prohibit further therapy.

**Progress :** No new patients entered in FY 95.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 91/008		<b>Status:</b> On-going	
<b>Title:</b> GOG 0026II: Trial of 5-Fluorouracil and High Dose Leucovorin in Advanced Metastatic or Recurrent Pelvic Malignancies					
<b>Start Date:</b> 10/19/90			<b>Est. Completion Date:</b> Ind x		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> pelvic malignancy,5-Fluorouracil,leucovorin:high dose					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$8000.00		02/05/93	

**Study Objective:** To implement a protocol to screen for activity and efficacy of new agents or combinations in patients with advanced or recurrent pelvic malignancies, resistant to higher priority methods of treatment. In this case, the agents are 5-FU and high dose Leucovorin.

**Technical Approach:** Patients who have received prior 5-FU are ineligible. Leucovorin will be administered in a dose of 200 mg/m<sup>2</sup> daily for 5 days and repeated at four and eight weeks and thereafter every five weeks. 5-FU will be administered in a dose of 370 mg/m<sup>2</sup>/day for 5 days, infused immediately after the Leucovorin has been given. An adequate trial will be defined as receiving one course of treatment and living four weeks for additional tumor assessment, provided death is not due to tumor progression. All patients entered on the study will be evaluated for toxicity. Patients will remain on study and continue receiving chemotherapy until disease progression or until toxicity prevents further treatment.

**Progress :** No new patients entered in FY 95.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 83/024		<b>Status:</b> Terminated	
<b>Title:</b> GOG 0026N: A Phase II Trial of Diahydroxyanthracenedione (DHAD) (NSC #30179) (CL232315) in Patients with Advanced Pelvic Malignancies					
<b>Start Date:</b> 11/19/82			<b>Est. Completion Date:</b> Indef.		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> COL William L. Benson, MC			COL Roger B. Lee, MC		
<b>Key Words:</b> cancer:pelvic,DHAD,diahydroxyanthracenedione					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		02/05/93	

**Study Objective:** To determine the efficacy of DHAD in patients whose advanced malignancies have been resistant to higher priority methods of treatment.

**Technical Approach:** All patients with measurable gynecological cancer who have failed higher prior therapies will be offered DHAD as a Phase II drug to determine its efficacy. The drug will be given as 12 mg/m<sup>2</sup> I.V. every three weeks. Patients will continue to receive the agent until progression or adverse effects prohibit further therapy. This protocol was closed to uterus/MMT patient entry in Aug. 87.

**Progress:** No patients were entered in this study during FY 93. In previous years, 3 patients were entered and have died of the disease. Protocol is terminated due on 7 Aug 1995 do to sufficient data collection.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 81/035		<b>Status:</b> On-going
<b>Title:</b> GOG 0041: Surgical Staging of Ovarian Carcinoma				
<b>Start Date:</b> 01/16/81		<b>Est. Completion Date:</b>		
<b>Department:</b> GOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> COL William L. Benson, MC		COL Roger B. Lee, MC		
<b>Key Words:</b> cancer:ovarian,surgical staging				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	02/05/93

**Study Objective:** To determine the spread of ovarian carcinoma to intraperitoneal structures and retroperitoneal lymph nodes by direct examination, cytologic sampling, and biopsy; to establish a surgical protocol for patients entered into GOG ovarian cancer treatments protocols; to determine the complication rate of the procedures.

**Technical Approach:** This protocol is being performed as a statistical protocol on patients who have surgery as standard treatment. Eligible patients will be those who have Stages I, II, or III ovarian carcinoma. Patients undergoing total abdominal hysterectomy, bilateral or unilateral salpingo-oophorectomy, bivalving of the ovary, selective pelvic and para-aortic lymphadenectomy, omental biopsy, or peritoneal cytology sampling will be studied. They will not be given any preoperative treatment, but will be subjected to a completed and thorough evaluation before surgery. All patients will be explored and the steps for surgery will be as standard surgery dictates. Specific observations will be made as to the findings. If fluid is not present, washings will be taken from the inside of the abdomen to study cells. A thorough examination of all structures from the diaphragm to the pelvic floor will be carried out. After surgical staging, patients will be transferred to the appropriate treatment protocol or to standard treatment if no protocol is available.

**Progress:** This study was closed to patient entry 12 Feb 87. Thirteen patients were enrolled, 2 have been lost to follow up, 3 have died, and 8 are still being followed.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 81/105		<b>Status:</b> On-going	
<b>Title:</b> GOG 0052: A Phase III Randomized Study of Cyclophosphamide Plus Adriamycin Plus Platinol Versus Cyclophosphamide Plus Platinol in Patients with Optimal Stage II Ovarian Adenocarcinoma					
<b>Start Date:</b> 08/21/81			<b>Est. Completion Date:</b> Mar 98		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> COL Roger B. Lee, MC			COL William L. Benson, MC LTC Gordon O. Downey, MC		
<b>Key Words:</b> Cancer:ovarian, adenocarcinoma, cyclophosphamide, Adriamycin, Platinol					
<b>Accumulative MEDCASE Cost:</b> \$0.00		<b>Est. Accumulative OMA Cost:</b> \$0.00		<b>Periodic Review:</b> 02/05/93	

**Study Objective:** To determine, in optimal Stage III ovarian adenocarcinoma, if the addition of adriamycin to cyclophosphamide plus cis-platinum improves progression-free interval, frequency of negative second-look laparotomy and survival. This protocol replaces GOG #25.

**Technical Approach:** Eligible patients are those more than six weeks post-operative with proven primary Stage III ovarian adenocarcinoma confined to the abdominal cavity and its peritoneal surfaces with residual tumor masses after surgery no larger than 1 cm in diameter. Patients with prior chemo or radiotherapy are ineligible. Patients will be randomized to cyclophosphamide plus Platinol every three weeks for eight courses or to cyclophosphamide and Platinol plus adriamycin every three weeks for eight courses. After eight courses those with less than clinically complete response will go off study and be followed for survival; those with clinically complete response will have second-look surgery to validate the complete response or to remove residual tumor masses. Patients will then be followed for approximately five years for survival rates.

**Progress:** This study was closed to patient entry, 20 Jul 85. Six patients were entered in the study and one is still being followed.

### Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 84/033

**Status:** On-going

**Title:** GOG 0072: Ovarian Tumors of Low Malignant Potential: A Study of the Natural History and a Phase II Trial of Melphalan and Secondary Treatment with Cisplatin in Patients with Progressive Disease

**Start Date:** 02/17/84

**Est. Completion Date:** Dec 88

**Department:** GOG

**Facility:** MAMC

**Principal Investigator:** LTC Mark E. Potter, MC

**Associate Investigators:**  
COL William L. Benson, MC

COL Roger B. Lee, MC

**Key Words:** tumor:ovarian,melphalan,cisplatin

**Accumulative**

**MEDCASE Cost:** \$0.00

**Est. Accumulative**

**OMA Cost:** \$0.00

**Periodic Review:**

02/05/93

**Study Objective:** To evaluate the biologic behavior of ovarian tumors of low malignant potential; to evaluate the effectiveness of chemotherapy against this disease (initially, a Phase II study of melphalan); and to evaluate the response rate to cisplatin in melphalan failures.

**Technical Approach:** Patients without prior chemotherapy or radiotherapy who have had adequate surgical staging will be eligible. Patients with no grossly visible residual disease will receive no treatment and be followed for 5 years if there is no subsequent disease. If there is no grossly visible clinically apparent residual for 12 months, the patients will have second look surgery and then proceed to melphalan treatment (5 days every four weeks) or follow-up (complete response). With progression after melphalan, patients will proceed to third look and cisplatin treatment (once every three weeks for eight weeks) or follow-up. If there is no evidence of response after three courses of cisplatin, the treatment will be discontinued. Patients who have progression during the first 12 months will be treated as above except they will proceed directly to melphalan treatment without second look surgery. Follow-up will be for a minimum of five years with clinical examination every three months for the first two years, then every six months thereafter.

**Progress:** This study was closed to patient entry 25 Feb 92. Ten patients were enrolled; 1 has died and 9 are still being followed.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 84/074		<b>Status:</b> On-going
<b>Title:</b> GOG 0078: Evaluation of Adjuvant VP-16, Bleomycin, and Cisplatin (BEP) Therapy in Totally Resected Choriocarcinoma, Endodermal Sinus Tumor, Embryonal Carcinoma and Grade 3 Immature Teratoma of the ...				
<b>Start Date:</b> 08/17/84		<b>Est. Completion Date:</b> Jul 89		
<b>Department:</b> GOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> COL William L. Benson, MC		COL Roger B. Lee, MC		
<b>Key Words:</b> cancer:ovarian,teratoma,tumor:sinus,chemo,bleomycin,cisplatin				
<b>Accumulative MEDCASE Cost:</b> \$0.00		<b>Est. Accumulative OMA Cost:</b> \$0.00		<b>Periodic Review:</b> 02/05/93

**Study Objective:** To evaluate the effect of adjuvant vinblastine, bleomycin, and cisplatin (VBP) chemotherapy in patients with endodermal sinus tumor and choriocarcinoma of the ovary (pure and mixed) after removal of all gross tumor; to evaluate the role of serum markers, especially alpha fetoprotein and HCG, in predicting recurrence; to evaluate the role of reassessment laparotomy in determining response, detecting early relapse, and planning further therapy; and to compare the biologic behavior of pure endodermal sinus tumors with mixed germ cell tumors containing endodermal sinus elements. Per addendum of Jan. 87: to evaluate the acute and chronic toxicity of this chemotherapy on gonadal and reproductive function.

**Technical Approach:** Patients with totally resected Stage I choriocarcinoma, endodermal sinus tumor, or embryonal carcinoma of the ovary with negative peritoneal washings, normal (or falling at a rate that does not suggest residual disease) serum AFP and beta-HCG levels, and adequate bone marrow, renal, and hepatic function will be studied. Stages II and III will also be eligible if all gross tumor is resected. After recovery from surgery, patients will receive 3 cycles of VBP therapy. Patients who show evidence of progression while on VBP therapy will be candidates for GOG Protocol 26. Patients completing three cycles of treatment clinically free of disease will undergo reassessment laparotomy. Patients with recurrent disease at reassessment laparotomy will be candidates for GOG Protocol 26. To be eligible a patient will receive at least one week of chemotherapy and live another two weeks. Each patient will remain on study until adverse effects prohibit further therapy or until evidence of progression is noted. Per addendum of Jan. 86: the title has been changed as shown above; vinblastine has been replaced by VP-16; Grade 3 immature teratoma has been added for entry and evaluation.

**Progress:** Closed to patient entry 10 Feb 92. One patient was enrolled in FY 92 and is still being followed.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 86/089	<b>Status:</b> On-going
<b>Title:</b> GOG 0085: A Randomized Comparison of Hydroxyurea versus 5-FU Infusion and Bolus Cisplatin as an Adjuvant to Radiation Therapy in Patients with Stages II-B, III, and IV-A Carcinoma of the Cervix and...		
<b>Start Date:</b> 08/15/86	<b>Est. Completion Date:</b> Feb 94	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Mark E. Potter, MC		
<b>Associate Investigators:</b> COL Roger B. Lee, MC		COL William L. Benson, MC LTC Gordon O. Downey, MC
<b>Key Words:</b> cancer:cervical, carcinoma, hydroxyurea, 5-FU, Cisplatin, radiotherapy		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 02/05/93

**Study Objective:** To determine whether hydroxyurea or the combination of 5-FU and cisplatin is superior as a potentiator of radiation therapy in advanced cervical carcinoma and to determine the relative toxicities of hydroxyurea versus the combination of 5-FU and cisplatin when given concurrently with radiation therapy.

**Technical Approach:** Patients with invasive squamous cell, adenocarcinoma, or adenosquamous carcinoma of the cervix, Stages II-B, III, and IV-A, who meet the eligibility requirements as listed in the protocol, will undergo clinical staging as permitted by FIGO rules. All patients will undergo surgical staging to include extraperitoneal sampling of the para-aortic lymph nodes, peritoneal cytology, and intraperitoneal exploration. Patients with cancer confined to the pelvis will receive pelvic irradiation and will be randomly assigned to receive either concomitant 5-FU and cisplatin or hydroxyurea. Patients with disease outside the pelvis are not eligible for this protocol. The study will continue as long as treatment protocols remain activated. The patients will be followed for two years and then every six months for three additional years.

**Progress:** This protocol was closed to patient entry in December 1990 because it was reported that the two patients entered on the study had died (at a different institution). After further review it was discovered that this was a mistake and the protocol was reopened in Feb 93. Two patients were entered at MAMC and are still being followed.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/093		<b>Status:</b> On-going	
<b>Title:</b> GOG 0087G: A Phase II Trial of Paclitaxel (Taxol) in Patients With Advanced or Recurrent Uterine Sarcomas					
<b>Start Date:</b> 04/01/94			<b>Est. Completion Date:</b> Apr 97		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Cancer:uterine, sarcoma, Paclitaxel					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	/ /	

**Study Objective:** To compare the efficacy of Paclitaxel (Taxol) in patients with advanced or recurrent uterine sarcomas.

**Technical Approach:** Patients eligible to participate in this study will be treated with Paclitaxel at 175 mg/m<sup>2</sup> given as a three hour infusion every three weeks. Infusion is administered intravenously after premedication with decadron, and H1 and H2 blockers. Weekly CBC's are monitored and patients will be subsequently treated with granulocyte-colony stimulator factor (G-CSF) support for prolonged neutropenia or febrile neutropenia. In the event of persistent neutropenia despite G-CSF support, dose reductions will occur. Patients who have received previous pelvic radiation therapy will be treated at a decreased dose of 135 mg/m<sup>2</sup>. In the event that tumor measurements are obtainable by either physical examination or routine radiographs, tumor measurement will be obtained every three weeks prior to therapy. If CT or ultrasound imaging is required for tumor measurements, tumor measurements will be obtained every six weeks. Patients will remain on study until disease progression or evidence of significant toxicity.

**Progress:** No patients have been enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 87/013	<b>Status:</b> On-going
<b>Title:</b> GOG 0090: Evaluation of Cisplatin, Etoposide, and Bleomycin (BEP) Induction Followed by Vincristine, Dactinomycin, and Cyclophosphamide (VAC) Consolidation in Advanced Ovarian Germ Cell Tumors		
<b>Start Date:</b> 10/17/86	<b>Est. Completion Date:</b> Indef.	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Mark E. Potter, MC		
<b>Associate Investigators:</b> COL William L. Benson, MC COL Roger B. Lee, MC		
<b>Key Words:</b> tumor:germ cell:ovary,cisplatin,etoposide,bleomycin,VAC,vincristine,dactinomycin,cyclophosphamide,BEP		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 02/05/93

**Study Objective:** To evaluate the effect of induction chemotherapy with cisplatin plus etoposide plus bleomycin (BEP) followed by consolidation with vincristine plus dactinomycin plus cyclophosphamide (VAC) in previously untreated patients with advanced ovarian germ cell tumors.

**Technical Approach:** After adequate recovery from surgery (if done) previously untreated patients will be treated by three courses of BEP followed by three courses of VAC. Patients exhibiting disease progression on either phase will be taken off study. Patients who had previous VAC or similar regimens will be treated with four courses of BEP. After recovery from BEP therapy, reassessment laparotomy will be performed in patients with negative markers who are clinically free of disease. Progressing patients will be removed from the study. Patients with no evidence of disease at second look will be followed. Patients with persistent disease at second look will be removed from the study. An adequate trial is defined as receiving two courses of the drug and living at least six weeks. Each patient will remain on study until adverse effects prohibit further therapy or until evidence of progression of disease.

**Progress:** No patients have been enrolled in this study.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 87/104		<b>Status:</b> On-going	
<b>Title:</b> GOG 0092: Treatment of Selected Patients with Stage 1B Carcinoma of the Cervix After Radical Hysterectomy and Pelvic Lymphadenectomy: Pelvic Radiation Therapy versus No Further Therapy					
<b>Start Date:</b> 08/21/87			<b>Est. Completion Date:</b> Indef.		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> COL William L. Benson, MC			COL Roger B. Lee, MC COL Donald H. Kull, MC		
<b>Key Words:</b> cancer:cervix,hysterectomy,lymphadenectomy,radiotherapy					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 02/05/93

**Study Objective:** To determine the value of adjunctive pelvic radiation in the treatment of Stage 1B carcinoma of the cervix but with selected high-risk factors; to determine the recurrence-free interval, survival and patterns of failure in those patients; and to determine the morbidity of adjunctive pelvic radiation following radical hysterectomy.

**Technical Approach:** All patients with Stage 1B cancer of the cervix who have been treated by radical hysterectomy and pelvic node dissection and found to have cancer confined to the cervix and who have a large tumor and/or lymph or blood vessel invasion in the cervix will be eligible to enter the study. Patients will be randomized to one of two groups. One group will receive external radiation therapy to the pelvis and the other group will receive no further therapy. Patients assigned to receive the radiation therapy will receive the therapy daily for 4 to 6 weeks. Both groups of patients will be required to have check-ups every three months for three years and then every six months for two more years.

**Progress:** Study is closed to patient entry on 18 Sep 1995. One patient was enrolled in FY 88 and is still being followed.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 89/036		<b>Status:</b> On-going	
<b>Title:</b> GOG 0093: Evaluation of Intraperitoneal Chromic Phosphate Suspension Therapy Following Negative Second-Look Laparotomy for Epithelial Ovarian Carcinoma (Stage III)					
<b>Start Date:</b> 03/17/89			<b>Est. Completion Date:</b> Indef.		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> cancer:ovarian,chromic phosphate,laparotomy					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$2416.00		02/05/93	

**Study Objective:** To evaluate the role of intraperitoneal chromic phosphate (32P) suspension therapy in patients with Stage III epithelial ovarian carcinoma who have no detectable evidence of disease at the second-look laparotomy and to evaluate disease free survival, sites and frequency of relapse, and the morbidity from intraperitoneal 32P therapy.

**Technical Approach:** Patients with primary histologically confirmed epithelial carcinoma of the ovary who are in complete clinical remission, with no persistent or recurrent cancer, and initial FIGO Stage III will be eligible. Patients with distant metastatic disease, previous pelvic or abdominal radiation therapy, previous or concomitant malignancies other than of skin (excluding melanoma), and borderline malignancy of the ovary will be ineligible. Patients will be randomized to one or two regimens. Regimen I will consist of 15 millicuries of intraperitoneal chromic phosphate suspension therapy, preferably within 10 days (but no more than six weeks) after second-look laparotomy. Patients will be randomized before second-look laparotomy and a dialysis catheter will be inserted during second-look laparotomy in those patients randomized to receive 32P. Patients will be rotated every 10 minutes (left side to back to right side) for two hours to facilitate distribution of the 32P. Anterior and lateral scans of the abdominal cavity will be done to evaluate adequate distribution in the peritoneal cavity of the 32P and to confirm that loculation has not occurred. Data collection will continue until disease progression or death.

**Progress:** No patients have been enrolled in this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 87/028		<b>Status:</b> On-going	
<b>Title:</b> GOG 0095: Randomized Clinical Trial for the Treatment of Women with Selected Stage IC and II (A,B,C) and Selected IAi and IBi and IAii and IBii Ovarian Cancer, Phase III					
<b>Start Date:</b> 11/21/86			<b>Est. Completion Date:</b> Indef.		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> COL William L. Benson, MC			COL Roger B. Lee, MC		
<b>Key Words:</b> cancer:ovarian,cyclophosphamide,cisplatin,P32					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	02/05/93	

**Study Objective:** In definitively staged patients who have tumor involving one or both ovaries with pelvic extension and/or malignant ascites and/or positive peritoneal washings and in those Stage IAi and IBi patients with poorly differentiated tumors and stage IAii and IBii (all grades) to: compare the progression-free interval and overall survival of the two treatment regimens; determine the patterns of relapse for each form of therapy; and define the relative toxicities of the two treatment approaches.

**Technical Approach:** The study design will be a randomized comparison between the standard adjuvant treatment (P32) and an experimental arm of short term intensive adjuvant combination chemotherapy with cyclophosphamide/cisplatin. One to two weeks following surgery, P32 therapy will be started. Fifteen millicuries of chromic phosphate suspension mixed in 500 cc of normal saline will be infused into the peritoneal cavity via the peritoneal dialysis catheter after a technetium scan or abdominal x-rays with contrast material has demonstrated adequate distribution. In order to facilitate distribution of the P32, the patient will be turned every 15 minutes to the left side, onto the back, in Trendelenburg and reverse Trendelenburg positions, onto the right side and so on for two hours following the infusion. Chemotherapy will consist of cyclophosphamide, 1 mg/m<sup>2</sup> I.V., on day 1 plus cisplatin, 100 mg/m IV, on day 1 administered one hour after cyclophosphamide. Cycles of combination chemotherapy will be repeated every three weeks depending upon the time to recovery of the blood counts to pretreatment level. Cycles of chemotherapy will be repeated for a total of three cycles. Patient follow-up will continue until death, loss of follow-up, or termination of the study. Patients will remain on study until disease progression or adverse effects dictate otherwise. An adequate trial is defined as receipt of at least one course of therapy and one follow-up visit.

**Progress:** This protocol was closed to patient entry 14 Mar 94. Five patients have been entered and 1 remains in follow-up.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 87/091		<b>Status:</b> On-going	
<b>Title:</b> GOG 0099: A Phase III Randomized Study of Adjunctive Radiation Therapy in Intermediate Risk Endometrial Adenocarcinoma					
<b>Start Date:</b> 06/19/87			<b>Est. Completion Date:</b> Indef.		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> COL William L. Benson, MC			COL Roger B. Lee, MC		
<b>Key Words:</b> cancer:endometrial,radiotherapy					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 02/05/93

**Study Objective:** To determine if patients with intermediate risk endometrial adenocarcinoma who have no spread of disease to the lymph nodes benefit from postoperative pelvic radiotherapy and to evaluate how the addition of pelvic radiotherapy will alter the site and rate of cancer recurrence in these intermediate risk patients.

**Technical Approach:** Patients with primary histologically confirmed Grade 2 or 3 endometrial adenocarcinoma (endometrioid, villoglandular, mucinous and adenosquamous) and clear cell carcinoma will be eligible. Patients must have had a total abdominal hysterectomy, bilateral salpingo-oophorectomy, selective pelvic and para-aortic node sampling, pelvic washings and found to be surgical Stage 1 with myometrial invasion. Following surgery, patients will be randomized to no additional treatment of pelvic radiation therapy to begin no later than eight weeks after surgery. Those randomized to radiation therapy will be treated with AP and PA parallel ports with each port being treated each day. A daily tumor dose of 180 cGy will be given to a total dose of 5040 cGY in approximately six weeks. Each patient will be followed with regular visits occurring every three months for the first two years, every six months for the third, fourth and fifth years, and yearly thereafter.

**Progress:** Closed to patient entry on 3 July 1995. One patient was enrolled at MAMC during FY 95. There are two patients enrolled in previous years that are being followed.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 89/052		<b>Status:</b> On-going	
<b>Title:</b> GOG 0108: Ifosfamide (NSC #109724) and the Uroprotector Mesna (NSC #113891) with or without Cisplatin (NSC #119875) in Patients with Advanced or Recurrent Mixed Mesodermal Tumors of the Uterus					
<b>Start Date:</b> 04/21/89			<b>Est. Completion Date:</b> Indef.		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> tumor:uterus,ifosfamide,cisplatin,uroprotector mesna					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		02/05/93	

**Study Objective:** To determine: whether the addition of cisplatin to doxorubicin offers significant improvement in the frequency of objective response; the duration of progression-free interval; and the length of survival as compared to doxorubicin alone.

**Technical Approach:** Patients will be randomized to either Regimen I or Regimen II. Regimen I: doxorubicin 60 mg/m<sup>2</sup> IV every three weeks to a maximum total dose of no greater than 500 mg/m<sup>2</sup>. Regimen II: doxorubicin 60 mg/m<sup>2</sup> IV every three weeks plus cisplatin, 50 mg/m<sup>2</sup> IV, every three weeks, to be continued to a maximum total dose of doxorubicin of 500 mg/m<sup>2</sup>. Each regimen will require both dose escalation and dose reduction in accordance with adverse effects observed on the previous course of therapy. Patients who reach maximum doxorubicin dose will undergo a complete re-evaluation. All therapy will then be stopped and the patient followed on no further therapy until progression of disease is documented. Further therapy at that point will be at the discretion of the investigator. Patients on no further treatment will be followed every three months for the first two years, then every six months for three years, and annually thereafter.

**Progress:** No patients were entered in this study at MAMC during FY 95.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 91/086		<b>Status:</b> On-going	
<b>Title:</b> GOG 0109 (SWOG 8797): A Randomized Comparison of 5-FU Infusion and Bolus Cisplatin as an Adjunct to Radiation Therapy, versus Radiation Therapy Alone in Selected Patients with Stages ...					
<b>Start Date:</b> 08/02/91			<b>Est. Completion Date:</b>		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> cancer:cervix, 5-Fluorouracil, cisplatin, radiotherapy					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	02/05/93	

**Study Objective:** To determine whether the combination of 5-fluorouracil (5-FU) and cisplatin used as an adjunct to radiation therapy will improve survival rate or progression-free survival and decrease extra pelvic failure compared to radiation therapy alone in patients with positive pelvic lymph nodes, positive parametrial involvement, or positive surgical margins following radical hysterectomy and lymph node dissection for Stages I-A2, I-B, and II-A carcinoma of the cervix and to determine the increase in toxicities due to 5-FU and cisplatin as an adjunct to radiation therapy versus radiation therapy alone.

**Technical Approach:** Patients must have primary, histologically confirmed, invasive squamous cell carcinoma, adenocarcinoma, or adenosquamous carcinoma of the uterine cervix, clinical stages I-A2, I-B, or II-A and must have had a radical hysterectomy with total pelvic lymphadenectomy and para-aortic sampling. Patients must have, at surgical evaluation, either histologically confirmed positive pelvic lymph nodes, positive parametrial involvement, or positive surgical margins. Patients with confirmed positive para-aortic lymph nodes are not eligible. Patients must not have received prior chemotherapy, immunotherapy (including biologics), hormonal therapy, or pelvic irradiation. Patients will be randomly assigned to receive either 5-FU and cisplatin plus pelvic irradiation or pelvic irradiation alone. Patients with positive high common iliac lymph nodes will receive extended field para-aortic irradiation. Irradiation and chemotherapy will begin simultaneously within six weeks after surgery. Chemotherapy will be given once a week every three weeks for four cycles. Radiation therapy will be given for six weeks. After completion of therapy, patients will be followed every 3 months for two years and every 6 months thereafter. Formal analysis of progression-free and overall survival will be performed at 2 1/2 years after the start of patient accrual to determine if consideration should be given to early termination of either treatment arm.

**Progress:** This study was closed to patient entry 20 May 94. No patients were enrolled at MAMC during FY 95. The one patient enrolled in previous years is still in follow-up.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 91/064	<b>Status:</b> On-going
<b>Title:</b> GOG 0113: An Evaluation of Hydroxyurea, 5-FU Infusion and Bolus Cisplatin as an Adjunct to Radiation Therapy in Patients with Stages II-B, III, and IV-A Carcinoma of the Cervix and Negative .....		
<b>Start Date:</b> 05/03/91	<b>Est. Completion Date:</b>	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Mark E. Potter, MC		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> cancer:cervix, hydroxyurea, 5-Fluorouracil, cisplatin		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	02/05/93

**Study Objective:** To evaluate the toxicity and feasibility of infusion 5-FU, cisplatin, and hydroxyurea, given concurrent with pelvic radiation therapy in patients with locally advanced cancer of the uterine cervix.

**Technical Approach:** Multiple studies have confirmed that the presence of metastases to para-aortic lymph nodes is a prognostic factor of greater significance than FIGO Stage. In addition, the pattern of failure in this group is vastly different, with one-half of the recurrences being outside the treated field. Because a major objective of this study is to evaluate local control and survival, this study will be open only to those patients with documented negative para-aortic nodes. All patients will undergo surgical staging to include extraperitoneal sampling of the para-aortic lymph nodes. Radiation therapy will be given by external beam therapy followed by intracavitary therapy. Cisplatin will be given IV on days 1 and 29 of external radiation therapy; 5-FU will be given IV on days 2, 3, 4, 5, 30, 31, 32, and 33 of external radiation therapy; and hydroxyurea will be given PO four days each week during external radiation therapy. After therapy, patients will be followed every three months for two years and then every six months for three years for progression free interval and survival.

**Progress:** This study was closed to patient entry, 15 Oct 91. Two patients were enrolled in FY 92 and still being followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/059		<b>Status:</b> Completed	
<b>Title:</b> GOG 0114: A Phase III Randomized Study of Intravenous Cisplatin and Cyclophosphamide vs Intravenous Cisplatin and Taxol vs High Dose Intravenous Carboplatin Followed by Intravenous Taxol and ....					
<b>Start Date:</b> 03/05/93			<b>Est. Completion Date:</b> Oct 96		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> cancer:ovarian carcinoma, cisplatin, cyclophosphamide, Taxol, carboplatin					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		/ /	

**Study Objective:** 1) To compare the efficacy of the combination of Cisplatin & Taxol to the standard therapy of Cyclophosphamide and Cisplatin in patients with optimally debulked Stage III Ovarian Carcinoma. 2) To investigate the theory that intravenous high dose therapy will render patients more sensitive to intraperitoneal therapy with Cisplatin and intravenous Taxol. The rate of fall of serum CA-125 will be correlated with response to chemotherapy.

**Technical Approach:** Patients who have had appropriate surgery for ovarian carcinoma with a histologic diagnosis of epithelial ovarian carcinoma, Stage III optimal, and who are not more than six weeks post-operative will be considered for this study. Upon entry, patients will be stratified according to whether or not gross residual disease is present (gross disease being any visible unresected tumor remaining after surgery). They will then be randomized to 1 of 3 regimens. Regimen I: - Cisplatin 75 mg/m<sup>2</sup> IV & Cyclophosphamide 750 mg/m<sup>2</sup> IV every 21 days X 6 courses. Regimen II: Taxol 135 mg/m<sup>2</sup> 24 hour continuous infusion, Day 1, Q 21 days followed by Cisplatin 75 mg/m<sup>2</sup>, Day 2 Q 21 days X 6 courses. Regimen III: Carboplatin (dose mg = target AUC X (GFR + 25) Q 4 weeks X 2 administered intraperitoneally through an implantable peritoneal dialysis catheter followed by Cisplatin 100 mg/m<sup>2</sup> intraperitoneally Q 21 days X 6 and Taxol 135 mg/m<sup>2</sup> IV X 6. While being treated, patients will have blood samples performed on a weekly basis to assess the serum CA-125 levels which will be correlated in response to chemotherapy. Response evaluations will be based on second-look surgical reassessment.

There will be two interim analyses conducted when approximately 188 patients and 375 patients are evaluable for second-look response. The critical values of the chi-square test statistic are 5.41, 5.41, and 3.283 at final analysis. These critical values correspond to the following probabilities (one-sided favoring the experimental therapy): 0.010, 0.010, and 0.035. The over-all error (rejecting either hypothesis) is 0.0754.

**Progress:** Study closed to patient entry on 3 April 1995. No patients have been enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 91/074		<b>Status:</b> On-going
<b>Title:</b> GOG 0115: Bleomycin (NSC #125066), Etoposide (NSC #141540) and Cisplatin (NSC #119875) (BEP) as First-Line Therapy of Malignant Tumors of the Ovarian Stroma (Granulosa Cell, Sertoli-Leydig Tumor, ...				
<b>Start Date:</b> 07/12/91		<b>Est. Completion Date:</b>		
<b>Department:</b> GOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> tumor:ovarian stroma,chemo,bleomycin,etoposide,cisplatin				
<b>Accumulative MEDCASE Cost:</b> \$0.00		<b>Est. Accumulative OMA Cost:</b> \$0.00		<b>Periodic Review:</b> 02/05/93

**Study Objective:** To assess the efficacy of bleomycin, etoposide (VP-16), and cisplatin (BEP) chemotherapy in patients with malignant tumors of the ovarian stroma as a first-line regimen.

**Technical Approach:** Eligible patients will be those with histologically confirmed primary Stages II, III, or IV with incompletely resected disease, recurrent or persistent tumor of the ovarian stroma (granulosa cell tumor, granulosa-theca cell tumor, Sertoli-Leydig cell tumor, androblastoma, gynandroblastoma, unclassified sex cord stromal tumor, or sex cord tumor with annular tubules). Patients will undergo, where appropriate, a total abdominal hysterectomy and bilateral salpingo-oophorectomy. Omentectomy, cytologic washings, and other surgical staging such as pelvic and peri-aortic node sampling, multiple pelvic and diaphragmatic node biopsies are optional. Within 8 weeks of surgery, patients will be placed on BEP therapy: bleomycin IV push weekly for nine weeks, etoposide IV daily times five every three weeks for four courses, cisplatin IV daily times five, every three weeks for four courses. Complete responders or patients with nonmeasurable disease will undergo reassessment laparotomy not later than eight weeks following final course of therapy. To be evaluable for response, a patient will receive at least one course of chemotherapy. The efficacy of the three-drug combination will be evaluated by frequency of negative second-look and frequency and severity of acute toxicity.

**Progress:** One patient was enrolled in this study in FY 95 and one patient was enrolled in FY 84. One is still being followed and the other was lost to follow-up.

### Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 94/013

**Status:** On-going

**Title:** GOG 0116: Evaluation of Adjuvant VP-16 and Carboplatin Therapy in Totally Resected Ovarian Dysgerminoma

**Start Date:** 10/01/93

**Est. Completion Date:** Apr 96

**Department:** GOG

**Facility:** MAMC

**Principal Investigator:** LTC Mark E. Potter, MC

**Associate Investigators:** None

**Key Words:** Cancer:ovarian, VP-16, carboplatin

**Accumulative**

**Est. Accumulative**

**Periodic Review:**

**MEDCASE Cost:** \$0.00

**OMA Cost:** \$0.00

//

**Study Objective:** To evaluate the efficacy and toxicity of adjuvant VP-16 and carboplatin in patients with totally resected ovarian dysgerminoma.

**Technical Approach:** Patients who have had totally resected Stage Ib-III ovarian dysgerminoma will be eligible for this study. Those patients will undergo chemotherapy utilizing VP-16 10 mg/m<sup>2</sup> on days 1-3 carboplatin 400 mg/m<sup>2</sup> on day 1. After completion of the chemotherapy, patients will be evaluated in follow-up every two months for one year, every three months for the second year, then every four to six months thereafter for a total of five years. At the completion of the five year follow-up annual evaluations will then be performed. At the time of each follow-up, physical examination, liver function tests, and tumor markers of Beta-HCG and Alpha-fetoprotein will be obtained.

**Progress:** No patients have been enrolled at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/061		<b>Status:</b> On-going	
<b>Title:</b> GOG 0120: A Randomized Comparison of Hydroxyurea vs Hydroxyurea, 5-FU Infusion and Bolus Cisplatin vs Weekly Cisplatin as Adjunct to Radiation Therapy in Patients with Stages IIB, III, IVA Carcinoma..					
<b>Start Date:</b> 03/05/93			<b>Est. Completion Date:</b> Oct 97		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> cancer:cervix, hydroxyurea 5-FU, cisplatin, radiation therapy					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		/ /	

**Study Objective:** 1) To compare the relative efficacy of radiation sensitization of hydroxyurea alone or in combination with 5-Fluorouracil and Cisplatin versus Cisplatin alone in the treatment of Stages II-B through IV-A carcinoma of the cervix. 2) To determine the relative toxicities of these three different radiation sensitization schemes.

**Technical Approach:** Patients with locally advanced carcinoma of the cervix who have histologically confirmed negative para-aortic lymph nodes will be eligible for this study. Patients who consent will be randomized to three different treatment regimens. All treatment regimens will include the same radiation therapy technique given as standard therapy. Randomization will be between 1) Cisplatin 40 mg/m<sup>2</sup> IV q week X 6, (2) Cisplatin 50 mg/m<sup>2</sup> IV on days 1 & 29 with continuous infusion of 5-FU 1000 mg/m<sup>2</sup> on days 2 - 5 and 30 - 33 and hydroxyurea PO 2 mg/m<sup>2</sup> Mon/Thurs every week during radiation therapy (3) hydroxyurea PO 3 gm/m<sup>2</sup> Mon/Thurs every week during radiation therapy. Following therapy, patients will be monitored every 3 months for first 2 years and then every 6 months for the next 3 years.

To determine the efficacy of cisplatin, the principle parameters to be collected, analyzed and reported are: a) outcome variables (recurrence-free interval and survival) b) tumor characteristics c) host characteristics d) adverse effects (frequency and severity e) therapy administered.

Interim analyses will be conducted at approximately the 2nd, 3rd, 4th and 5th years using a global log-rank test. The goal will be to identify large differences in the recurrence free interval among the three treatment regimens. The interim log-rank test will be adjusted for important prognostic factors. The critical values of the chi-square test statistics are 11.1, 10.8, 10.6, 10.6, and 3.81. The last critical value is for the final analysis which will be a one-sided pair-wise test. These critical values correspond to the following tail probabilities from the two degrees of freedom chi-square distribution: 0.0039, 0.0045, 0.0050 and 0.0050. This early stopping rule will increase the type I error from 0.025 to 0.0386 for each test. The over-all type I error will be 0.0757.

**Progress:** No patients were enrolled at MAMC during FY 95

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/014		<b>Status:</b> On-going
<b>Title:</b> GOG 0122: Whole Abdominal Radiotherapy Versus Combination Doxorubicin-Cisplatin Chemotherapy in Advanced Endometrial Carcinoma				
<b>Start Date:</b> 10/01/93		<b>Est. Completion Date:</b> Jan 97		
<b>Department:</b> GOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> Cancer:endometrial, radiotherapy, doxorubicin, cisplatin				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>
\$0.00		\$0.00		//

Study Objective: 1) To compare the effectiveness of chemotherapy to whole abdominal radiation therapy in patients with advanced endometrial cancer which has been resected to less than 2 cm residual tumor. 2) To compare the relative toxicity of these two treatment strategies.

Technical Approach: Patients who have had surgical intervention for advanced (Stage III or IV) endometrial carcinoma confined to the abdominal cavity will be randomized either to whole abdominal radiation therapy or chemotherapy utilizing Doxorubicin at 60 mg/m<sup>2</sup> and Cisplatin at 50 mg/m<sup>2</sup> given every three weeks for eight cycles. After the completion of therapy patients will be seen and evaluated every three months for two years and six months thereafter for five years after treatment. Nationally 240 patients will be enrolled over 4 years. Patients will be evaluated for length of survival, disease-free survival and toxicity.

Progress: No patients have been enrolled in this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/063		<b>Status:</b> On-going	
<b>Title:</b> GOG 0123: A Randomized Comparison of Radiation Therapy & Adjuvant Hysterectomy vs Radiation Therapy & Weekly Cisplatin & Adjuvant Hysterectomy in Patients with Bulky Stage IB Carcinoma of the Cervix					
<b>Start Date:</b> 03/05/93			<b>Est. Completion Date:</b> Oct 97		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> cancer:cervix, radiation therapy, cisplatin, hysterectomy					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		//

**Study Objective:** To evaluate the addition of weekly chemotherapy with Cisplatin during radiation therapy in patients with bulky Stage IB carcinoma of the cervix.

**Technical Approach:** This study randomizes patients to two different treatment regimens. Both regimens include radiation therapy followed by hysterectomy. Regimen I - Radiation Therapy Plus Adjuvant Hysterectomy - Patients will undergo combined external and intracavitary radiation therapy followed by extrafascial hysterectomy (total doses of 13000 cGy). Regimen II - Radiation Therapy Plus Weekly Cisplatin Infusion Plus Extrafascial Hysterectomy. Patient will undergo radiation therapy to receive a total dose of 13000 cGy using a combination of external and intracavitary radiation therapy. Each week during external radiation therapy and during the intracavitary applications the patient will receive an infusion of cisplatin 40 mg/m<sup>2</sup> not to exceed 70 mg maximum in any single infusion, up to a maximum of 6 doses of cisplatin. Extrafascial hysterectomy will be carried out no later than six weeks following the last day of treatment in both regimens.

The principal parameters to determine the efficacy of weekly cisplatin during radiotherapy are: 1) Outcome variables (recurrence-free interval (RF), survival and local control rate); 2) Tumor characteristics; 3) Host characteristics; 4) Adverse effects; 5) Therapy administered

**Progress:** No patients have been enrolled at MAMC.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/064		<b>Status:</b> On-going
<b>Title:</b> GOG 0126C: A Phase II Evaluation of Altretamine (Hexamethylmelamine) in Recurrent, Platinum-Resistant and Refractory Ovarian Cancer				
<b>Start Date:</b> 01/20/95		<b>Est. Completion Date:</b> Aug 95		
<b>Department:</b> GOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> Cancer:ovary, altretamine				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//

Study Objective : To evaluate the use of altretamine as second-line chemotherapy in patients resistant to platinum containing compounds and taxol.

Technical Approach : Patients with epithelial ovarian cancer refractory to platinum containing compounds and taxol will be eligible for participation in this study. Participants in this study will be treated with altretamine at a dose of 260 mg/m<sup>2</sup> daily for 14 days. Treatment cycles will be repeated at 28 day intervals, providing serious side effects or tumor progression do not interfere. During the course of therapy weekly CBC's and liver function tests will be obtained. Should disease progression or severe side effects occur, therapy will be discontinued. Patients will be continued to be followed for life.

Progress: No patients have been enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/150		<b>Status:</b> Completed	
<b>Title:</b> GOG 0127C: Evaluation of Cisplatin and Pentoxifylline in Advanced or Recurrent Squamous Cell Carcinoma of the Cervix					
<b>Start Date:</b> 08/06/93			<b>Est. Completion Date:</b> Aug 94		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> cancer:cervix, cisplatin, pentoxifylline					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		/ /	

Study Objective: 1. To determine if the addition of methylxanthine pentoxifylline enhances the cytotoxicity of cisplatin in patients with recurrent or advanced squamous cell carcinoma of the cervix. 2. To determine if the side effects when combining pentoxifylline with cisplatin are acceptable.

Technical Approach: Patients with measurable, recurrent or advanced squamous cell carcinoma of the cervix consenting to participate will be entered into a treatment regimen consisting of cisplatin 75 mg/m<sup>2</sup> given every three weeks. Pentoxifylline will be given at 1600 mg orally every eight hours for nine doses (3 days). Treatment will continue for six cycles or until progression or toxicity precludes further therapy.

Progress: This study was closed to patient entry 21 Nov 94. No patients entered this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/071		<b>Status:</b> Completed
<b>Title:</b> GOG 0127F: Evaluation of Topotecan (NSC #609699) in Persistent or Recurrent Squamous Cell Carcinoma of the Cervix				
<b>Start Date:</b> 01/20/95		<b>Est. Completion Date:</b> Jan 96		
<b>Department:</b> GOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> Cancer:cervix, topotecan				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//

**Study Objective:** To evaluate the safety and efficacy of Topotecan in the treatment of patients with recurrent or metastatic squamous cell carcinoma unresponsive to traditional therapy.

**Approach:** Approximately two patients with metastatic or recurrent squamous cell carcinoma which have failed traditional therapy are eligible for this protocol. Generally since the GOG has protocols open for the treatment of chemotherapy naive patients, most patients entered into this study will have received previous chemotherapy as well as therapy directed at their primary tumor. Patients entered into this protocol will receive a daily infusion of topotecan administered intravenously for five consecutive days. The administration of the topotecan is delivered over 30 minutes. Toxicity will be monitored and patients continued on study until any cancer progression is noted or severe toxicity limits further treatment. During the course of chemotherapy cycle dosing will be adjusted based on toxicity criteria. If the white blood cell toxicity is the primary toxicity, the initial adjustment would be for a dose reduction. However, if continued dose adjustments are required or febrile neutropenia occurs, G-CSF will be administered. The G-CSF will be administered the day after the Topotecan is finished and continued until day 18 or until the white blood cell count recovers. The principal parameters employed to evaluate the efficacy of each agent are: frequency and duration of objective response, frequency and severity of observed adverse effects, survival time, duration of progression-free interval.

**Progress:** This study was closed to patient entry on 13 Apr 1995. No patients have been enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/171		<b>Status:</b> On-going
<b>Title:</b> GOG 127H: Evaluation of Prolonged Oral Etoposide (VP-16) in Persistent or Recurrent Squamous Cell Carcinoma of the Cervix				
<b>Start Date:</b> 07/21/95		<b>Est. Completion Date:</b> Sep 96		
<b>Department:</b> GOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> Cancer:cervix, squamous cell, etoposide				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	/ /

**Study Objectives:** To evaluate the safety and efficacy of prolonged oral VP-16 in the treatment of recurrent or metastatic squamous cell carcinoma of the cervix.

**Technical Approach:** Patients with historically proven or metastatic squamous cell carcinoma of the cervix will be treated with oral VP-16 for 21 consecutive days out of a 28 day cycle. Treatment will be reviewed on day 29 after a one week break. Patients who have received previous radiation therapy will be started at a lower dose initially. Dose modification with either dose reduction or dose intensification is possible depending on marrow rescue. Clinical management, including physical examination and chest x-ray will be obtained prior to each cycle. If additional imaging studies, such as CT ultrasound or MR are required, tumor measurements will be repeated after every other cycle. Treatment will be discontinued should severe toxicity or tumor progression result. There are no treatment comparisons involved and no known historical controls available. The study design will be primarily based on prior GOG experience in this disease entity. This will insure consistency in evaluation of response. therapy plans demonstrating activity will later be compared and investigated in ensuing phase III studies.

**Progress:** No patients have been enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/102		<b>Status:</b> On-going
<b>Title:</b> GOG 0128B: Evaluation of Paclitaxel (Taxol) in Persistenet or Recurrent Non-Squamous Cell Carcinoma of the Cervix and Vagina				
<b>Start Date:</b> 05/06/94		<b>Est. Completion Date:</b> May 95		
<b>Department:</b> GOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> Cancer:cervix, Cancer:vagina, paclitaxel				
<b>Accumulative MEDCASE Cost:</b> \$0.00		<b>Est. Accumulative OMA Cost:</b> \$0.00		<b>Periodic Review:</b> / /

**Study Objective:** To evaluate efficacy of Paclitaxel (Taxol) in the treatment of patients with persistent or recurrent non-squamous cell carcinoma of the cervix or vagina.

**Technical Approach:** Patients with incurable recurrent or persistent non-squamous cell carcinoma of the cervix and vagina are eligible to participate in this study. All patients will receive a 24 hour infusion of Paclitaxel at 170 mg/m<sup>2</sup> every three weeks. Patients who have received previous radiation therapy to the pelvis will be treated at a dose of 135 mg/m<sup>2</sup> every three weeks. Routine weekly CBCs will be obtained to monitor for significant neutropenia. Should significant neutropenia develop resulting in fever or prolonged neutropenia, dose reduction will occur. If a dose of 110 mg/m<sup>2</sup> still results in significant neutropenia, granulocyte colony stimulating factor (G-CSF) will be used. On subsequent treatment cycles, 5 microgram/kg will be administered subcutaneously starting 24 hours after therapy and continuing until absolute granulocyte count is sufficient. Patients will continue to receive Taxol every three weeks until tumor progression occurs or severe side effects prevent further therapy. Tumor measurements will be obtained prior to every cycle if detectable on physical examination. Measurements determined by x-rays or imaging studies will be obtained every 6 weeks.

**Progress:** No patients were enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/027		<b>Status:</b> On-going	
<b>Title:</b> GOG 0130B, Evaluation of Paclitaxel (Taxol) in the Treatment of Persistent or Recurrent Mixed Mesodermal Tumors of the Uterus.					
<b>Start Date:</b> 11/18/94			<b>Est. Completion Date:</b> JAN 96		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Mesodermal Tumors of the Uterus					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	/ /	

Study Objectives: To evaluate the efficacy of taxol in the treatment of mixed mesodermal tumors of the uterus.

Technical Approach: Patients with recurrent mixed mesodermal tumors of the uterus who have failed previous therapy are eligible to participate in this study. All patients entered in this study must have clinically or radiologically measureable tumors. Patients will be treated with a 24 hour infusion of paclitaxel at  $170 \text{ mg/m}^2$  intravenously. This therapy will be repeated every three weeks until the tumor progresses, side effects intervene, or the patient elects to withdraw from therapy. If the tumor is measureable by physical examination, tumor measurements will be obtained prior to each course of chemotherapy. If, however, radiological investigations are required for determining tumor size, imaging will be performed every 6 weeks. All patients will be treated until disease progression or severe side effects limit subsequent therapy. Annual accrual of approximately 15 patients is expected and approximately 40 are needed for the study.

Progress: No patients have been enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/062		<b>Status:</b> On-going
<b>Title:</b> GOG 0131B: Evaluation of Prolonged Oral Etoposide (VP-16) in the Treatment of Recurrent or Advanced Leiomyosarcoma of the Uterus				
<b>Start Date:</b> 02/04/94		<b>Est. Completion Date:</b> Jun 95		
<b>Department:</b> GOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> Cancer:uterus, leiomyosarcoma, etoposide				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//

**Study Objective:** To determine if the utilization of semi-continuous low dose oral etoposide has significant activity with an acceptable level of toxicity in patients with advanced or recurrent Leiomyosarcoma of the uterus who have failed standard therapy.

**Technical Approach:** Patients with histologically confirmed recurrent or metastatic leiomyosarcoma that have failed local therapeutic measures and have adequate bone marrow, renal, and hepatic function will be invited to participate in this study. Etoposide (VP-16) will be administered at a dosage of 50 mg/m<sup>2</sup>/day, day 1-21 every 4 weeks. If side effects are not severe, a patient may remain on the study agent indefinitely at the investigator's discretion. Likewise, patients with evidence of progressive disease or those with significant side effects or deterioration of performance status may be removed from study at the investigator's discretion. All patients will be followed until death.

**Progress:** No patients have been entered at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/023		<b>Status:</b> On-going	
<b>Title:</b> GOG 0132: A Phase III Randomized Study of Cisplatin versus Taxol versus Taxol and Cisplatin in Patients with Suboptimal Stage III and IV Epithelial Ovarian Carcinoma					
<b>Start Date:</b> 11/06/92			<b>Est. Completion Date:</b> Oct 95		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> cancer:ovarian, taxol, cisplatin					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	/ /	

**Study Objective:** To compare the efficacy of Cisplatin and Taxol alone and together in the treatment of advanced suboptimal Stages III or IV epithelial ovarian carcinoma and to determine which of the three regimens contributes most favorably to progression-free interval and survival.

**Technical Approach:** Patients with suboptimal Stages III or IV epithelial ovarian carcinoma will be randomized into one of three treatment regimens. Regimen I will be Cisplatin only, Regimen II Taxol only and Regimen III taxol plus Cisplatin. Patients will receive the chemotherapeutic regimen assigned at 21 day intervals for six cycles. Patients with clinical evidence of disease are strongly encouraged to undergo a second look laparotomy to assess response to treatment. Additionally patients will be followed for disease and survival.

The median time to progression for these women treated with a cisplatin-based regimen is 10.4 and 14.4 months with measurable disease and non-measurable disease respectively. The median time to death is 18.5 and 22.5 months respectively. The expected response rate in those women with measurable disease is 60%.

If one of these treatment regimens can increase the median time to progression by 40% (28.6% decrease in the relative failure rate), then this is considered clinically significant. A 30-month accrual period (600 patients) with an additional 12-month follow-up period will provide an 82.5% chance of detecting that one of these regimens provides this magnitude of treatment effect while limiting the type I error to 0.05. The null hypothesis being: the failure rates in each of the three treatment arms are equal.

There is an 80% chance of rejecting the null hypothesis significance if one of these regimens increases the frequency of clinical response by 19% (i.e. 60% to 79%) while limiting the type I error to 0.05.

**Progress:** This study was closed to patient entry May 94. Study was revised and reopened on 3 Jan 95. No patients have been enrolled in this study at MAMC.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/006		<b>Status:</b> Completed	
<b>Title:</b> GOG 0134: A Phase III Trial of Taxol at Three Dose Levels and G-CSF at Two Dose Levels in Platinum-Resistant Ovarian Carcinoma					
<b>Start Date:</b> 10/02/92			<b>Est. Completion Date:</b> Oct 95		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> cancer:ovarian, Taxol					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		/ /	

**Study Objective:** 1. To determine if the dose of taxol affects response rate, progression free interval or survival in patients with platinum-resistant ovarian cancer. 2. To compare the toxicities of the three regimens. 3. To compare the efficacy and toxicity of two dose levels of G-CSF (5 ug/kg/day versus 10 ug/kg/day) in patients who receive the highest taxol dose (250 mg/m<sup>2</sup>). 4. To determine the relationship between peak taxol plasma concentration and toxicity/response.

**Technical Approach:** Patients with platinum-resistant ovarian carcinoma will be stratified according to the presence of measurable disease. They will then be randomized to Regimen I, II, IIIa, or IIIb. Regimen I: Taxol 135 mg/m<sup>2</sup> by 24 continuous infusion, Day 1, every 21 days x 6 doses. Regimen II: Taxol 175 mg/m<sup>2</sup> by 24 hr continuous infusion, Day 1, every 21 days x 6 doses. Regimen IIIa: Taxol 240 mg/m<sup>2</sup> by 24-hour continuous infusion Day 1 and G-CSF 5 ug/kg/day day 3 through the nadir until ANC is greater than or equals 10,000/ul, every 21 days. Regimen IIIb: Taxol 250 mg/m<sup>2</sup> by 24-hour continuous infusion Day 1 and G-CSF 10 ug/kg/day Day 3 through the nadir until ANC is greater or equals 10,000/ul, every 21 days. At the completion of six courses of therapy surgical reassessment, if done, should be performed in those patients with clinically complete responses within eight weeks following the last cycle of chemotherapy. Minimum length of trial to evaluate response is defined as receiving one course of therapy and surviving three weeks for repeat measurement to be performed.

**Progress:** This study was closed to patient entry on 6 Feb 95. No patients have been enrolled in this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/139		<b>Status:</b> On-going	
<b>Title:</b> GOG 0137: A Randomized Trial of Estrogen Replacement Therapy Versus No Estrogen Replacement in Women With Stage I or II Endometrial Adenocarcinoma					
<b>Start Date:</b> 06/09/93			<b>Est. Completion Date:</b> Nov 20		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> cancer:endometrial, estarogen replacement					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		//

Study Objective: To determine if the use of estrogen replacement therapy significantly increased the risk of developing recurrence of endometrial cancer after primary treatment.

Technical Approach: Patients entered into this study will be have endometrial cancer without evidence of metastatic disease beyond the uterus or cervix. Some patients will have been simultaneously entered into a protocol randomizing them to receive radiation or no radiation. Other patients will have received treatment with or without radiation as recommended by their primary physician and/or choice. Patients who are randomized to estrogen replacement therapy will be taking estrogen on a daily basis for the duration of the study. Starting @ .625 mg per day and increasing to a maximum of 1.25 mg per day as needed for hot flashes. Patients who do not receive estrogen replacement therapy will have blood samples obtained every 3 - 6 months for serum estradiol levels to insure the exclusion of an external source of estrogen. All patients will receive yearly mammograms. All other follow up is in a standard fashion.

Progress: No patients have been enrolled in the study at MAMC.

### Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 93/087

**Status:** On-going

**Title:** GOG 0139: A Randomized Study of Doxorubicin Plus Cisplatin versus Circadian-Timed Doxorubicin Plus Cisplatin in Patients with Primary Stages III and IV, Recurrent Endometrial Adenocarcinoma

**Start Date:** 04/02/93

**Est. Completion Date:** Mar 96

**Department:** GOG

**Facility:** MAMC

**Principal Investigator:** LTC Mark E. Potter, MC

**Associate Investigators:** None

**Key Words:** Cancer:endometrial, doxorubicin, cisplatin, circadian timed doxorubicin

**Accumulative**

**Est. Accumulative**

**Periodic Review:**

**MEDCASE Cost:** \$0.00

**OMA Cost:** \$0.00

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**Study Objective:** 1. To evaluate the potential benefit of the administration of Circadian-timed, chemotherapy versus standard administration of chemotherapy utilizing Doxorubicin and Cisplatin. 2. To evaluate the relative toxicities of these two techniques of administration.

**Technical Approach:** This study will assess the relative benefit either in improved response rate or decreased toxicity by changing the method of delivery of the chemotherapeutic agents from an arbitrarily administered event to a timed delivery method. Patients will be randomized to receive either standard Doxorubicin/Cisplatin infusions given at a dose of Doxorubicin 60 mg per meter squared, IV Push followed by Cisplatin 60 mg per meter squared over 30 minutes immediately following the Doxorubicin in one treatment regimen as opposed to Doxorubicin at the same dose given IV Push over 30 minutes at 6 a.m. with the Cisplatin at 60 mg per meter squared delivered over 30 minutes at 6 p.m. Both chemotherapeutic regimen would be delivered every 3 weeks for a maximum of eight treatments. Dose reduction would occur initially because of advanced age or previous pelvic radiation therapy. Only patients with advanced or recurrent measurable Adenocarcinoma, Adenoacanthoma, Adenosquamous carcinomas, whose potential for cure by radiation therapy or surgery, alone or in combination is very poor. Prior to each cycle of chemotherapy, patients will be evaluated by history, physical examination, and the usual radiologic test required for monitoring tumor response. The treatment will continue for a maximum of eight treatments or until the tumor progresses.

**Progress:** No patients entered this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/140		<b>Status:</b> On-going	
<b>Title:</b> GOG 0140: An Assessment of Age and Other Factors Influencing Protocol Versus Alternative Treatments for Patients With Epithelial Ovarian Cancer Referred to Gynecologic Oncology Group Institutions					
<b>Start Date:</b> 06/09/93			<b>Est. Completion Date:</b> May 94		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> cancer: ovarian, protocol enrollment					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		//

Study Objective: To evaluate the reasons for inclusion or exclusion from GOG protocol studies.

Technical Approach: All patients with epithelial ovarian carcinoma, including borderline tumors who are primarily evaluated at MAMC will be eligible for participation in this study. All patients who have signed an informed consent will then have a questionnaire filled out regarding the relevant clinical material as well as selected underlying medical conditions; age, education, race, marital status, gravida and parity. Reasons for exclusion, either medical or other will be listed. Type of initial surgery performed, location of the surgery and types of subsequent therapy will also be entered on this questionnaire. After the completion of this study, which will include 800 subjects nationally, a GOG statistical office will analyze the data. Follow up of these patients is not a requirement of this study.

Progress: No patients entered this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/149		<b>Status:</b> Suspended	
<b>Title:</b> GOG 0143: Familial and Reproductive Factors in Ovarian Cancer					
<b>Start Date:</b> 08/06/93			<b>Est. Completion Date:</b> Aug 95		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> cancer: ovarian, familial factors, reproductive factors					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//	

**Study Objective:** 1. To further define the epidemiologic pattern of patients with invasive ovarian carcinoma. 2. To store genetic material for comparison should a genetic marker be identified in the future utilizing risk factors for the development of ovarian cancer to target a patient population suitable for screening.

**Technical Approach:** Patients identified with invasive ovarian carcinoma will be asked to complete a questionnaire. Additionally, two tubes of blood will be obtained and forwarded for storage, for potential DNA analysis. This is an epidemiologic study and requires no follow-up of the patients.

**Progress:** No patients entered this study at MAMC. Protocol was suspended July 1994, awaiting further instructions from GOG.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/140		<b>Status:</b> On-going	
<b>Title:</b> GOG 0145: A Randomized Study of Surgery vs Surgery + Vulvar Radiation in the Management of Poor Prognosis Primary Vulvar Cancer and of Radiation vs Radiation & Chemotherapy for Positive Inguinal Node					
<b>Start Date:</b> 08/05/94			<b>Est. Completion Date:</b>		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Cancer:vulvar, positive inguinal nodes					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		//

**Study Objective:** 1. To determine whether the additional radiation therapy to the area of vulvar resection decreases the risk of recurrent cancer in high risk patients. 2. Whether the addition of chemotherapy along with radiation improves the effect of radiation therapy in decreasing the risk of tumor recurrence in the areas treated by radiation therapy. 3. To evaluate the impact of these therapeutic interventions on the overall quality of life both during and subsequent to treatment. 4. To determine if HPV status alters the risk of local recurrence and/or survival.

**Technical Approach:** Patients with invasive squamous cell carcinoma of the vulva who meet the eligibility criteria will have initial surgery on the vulva and groins. After pathological examination of the specimen, patients will be eligible for randomization to observation or to additional therapy to the vulva. Patients with positive nodes will be randomized to receive radiation alone or radiation and chemotherapy to the inguinal and pelvic nodes. Patient treated with chemotherapy will receive Cisplatin day one, followed by four days of continuous infusion of 5 FU. In addition, patients will complete quality of life questionnaires prior to receiving radiation or chemotherapy, then at three, six, twelve, eighteen, and twenty-four months. All patients will be followed in the OB-GYN Oncology Clinic subsequent to treatment. Initial frequency of follow-up will be at three month intervals for one year, followed by four month intervals for one additional year and then every six months for an additional three years. The patient's disease status will be correlated with the presence or absence of HPV in the tumor and surrounding tissue.

**Progress:** No patients have been enrolled in this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/103		<b>Status:</b> Completed	
<b>Title:</b> GOG 0146B: Evaluation of Tomudex (ZD1694) (NSC #639186) in Recurrent, Platinum-Sensitive Ovarian Cancer					
<b>Start Date:</b> 05/06/94			<b>Est. Completion Date:</b> May 96		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Cancer:ovarian, Tomudex					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	/ /	

**Study Objective:** To identify effective agents for the treatment of epithelial ovarian cancers.

**Technical Approach:** Patients who agree to participate in this study will be treated with Tomudex, an investigational chemotherapeutic agent. Tomudex is a specific Thymidylate Synthase inhibitor. This treatment, administered every three weeks, is given as intravenous infusions over 15-30 minutes. Toxicity will be monitored with serial history and physical examinations, CBCs, liver function tests, and tumor measurements. Diagnostic imaging studies will be performed every six weeks, if necessary, to evaluate tumor response and then three weeks after treatment. Upon evidence of progressive disease or significant toxicity, treatment will be discontinued and an alternative treatment plan will be determined.

**Progress:** Study was closed to patient entry on 1 May 1995. No patients have been enrolled in this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/090		<b>Status:</b> On-going	
<b>Title:</b> GOG 0146C: Evaluation of Topotecan (SKF 104864-A) (NSC#609699) in Recurrent, Platinum, Sensitive Ovarian Cancer					
<b>Start Date:</b> 03/17/95			<b>Est. Completion Date:</b> Dec 95		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Cancer:ovarian, Topotecan, Platinum-Sensitive					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		//

**Study Objective:** To evaluate the safety and efficacy of Topotecan in the treatment of platinum-sensitive epithelial ovarian carcinoma.

**Approach:** Patients with recurrent epithelial ovarian cancer who have previously responded in a favorable fashion to platinum containing compounds will be eligible for this study. Patients who choose to participate will be treated with Topotecan, administered intravenously over thirty minutes daily for five consecutive days. Treatment cycles will be repeated every three weeks from the first day of chemotherapy. During the course of therapy, patients will have weekly CBC's and platelet counts. Prior to each course of treatment a history and physical examination will be preformed and routine liver function test (i.e., PT and PTT) will be obtained. Additionally, routine blood chemistries will be obtained. Tumor measurements will be obtained every three weeks if measurable on physical examination or routine chest radiography, however, if measured by CT or ultrasound it will be evaluated every six weeks. Patients will continue to receive chemotherapy every three weeks until tumor progression or severe toxicity intervenes. Patients who develop febrile neutropenia or develop neutropenia long enough to result in repetitive delays will be supported with Granulocyte-Colony Stimulating Factor (G-CSF) at 5 mcg/kg/day subcutaneously. G-CSF support will be administered the day after the last dose of Topotecan and continued through day 18 or until hematopoietic recovery. No G-CSF will be administered when the white blood cell count is greater than or equal to 15,000/mcL. Patients entered into this protocol will be followed for life.

**Progress:** No patients have been enrolled at MAMC.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/076	<b>Status:</b> Completed
<b>Title:</b> GOG 0147: A Quality of Life Companion Study to GOG 122 - Whole Abdominal Radiotherapy versus Combination Doxorubicin-Cisplatin Chemotherapy in Advanced Endometrial Carcinoma		
<b>Start Date:</b> 04/01/94	<b>Est. Completion Date:</b> Jan 97	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Mark E. Potter, MC		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> Cancer:endometrial, quality of life		
<b>Accumulative</b> <b>MEDCASE Cost:</b>	<b>Est. Accumulative</b> <b>OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	/ /

**Study Objective:** To evaluate the quality of life of patients entered into protocol GOG #122, Whole Abdomen Radiotherapy versus Combination Doxorubicin-Cisplatin Chemotherapy in advanced Endometrial Carcinoma.

**Technical Approach:** This is a quality of life protocol which evaluates patients already entered into protocol therapy on GOG protocol #122. Questionnaires will be administered pre treatment, post treatment, at 3, 6, and 12 month intervals and then yearly thereafter for three additional years. Data interpretation will be performed by the sponsor.

**Progress:** Study was closed to patient entry 24 Oct 1994. No patients have been entered at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/094	<b>Status:</b> On-going
<b>Title:</b> GOG 0148: The Clinical Utility of Soluble TNF/LT Membrane Receptors in the Serum of Patients With All Stages of Primary Epithelial Ovarian Cancer		
<b>Start Date:</b> 04/01/94	<b>Est. Completion Date:</b> May 95	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Mark E. Potter, MC		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> Cancer:ovarian, membrane receptors, tumor necrosis factor, lymphotoxin		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> / /

**Study Objective:** To evaluate the clinical utility of TNF/LT membrane receptor levels in the serum of patients with epithelial ovarian cancers as both a screening test and marker of therapeutic effect.

**Technical Approach:** This investigation will follow serum TNF/LT membrane receptors in the serum of patients who are undergoing treatment for primary epithelial ovarian cancer under other GOG protocols. Serum will be obtained prior to the first cycle of chemotherapy and then every other cycle thereafter. After the completion of chemotherapy, serum will be obtained every six months for two additional years. In the event that recurrent disease is suspected, serum will be obtained for investigation. The serum samples will be obtained at the time of routine laboratory studies utilized in the monitoring of ovarian cancer patients. No additional phlebotomy is therefore required.

**Progress:** No patients have been enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/061		<b>Status:</b> On-going	
<b>Title:</b> GOG 0150: A Phase III Randomized Study of Accelerated Hyperfractionated Whole Abdominal Radiotherapy (AHWAR) vs Combination Ifosfamide-Mesna With Cisplatin ... Carcinosarcoma (CS) of the Uterus					
<b>Start Date:</b> 02/04/94			<b>Est. Completion Date:</b> Feb 00		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Cancer:uterine, ifosfamide,mesna, cisplatin, abdominal radiotherapy					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		/ /	

**Study Objective:** To compare the use of combination Ifosfamide with Mesna and Cisplatin to hyperfractionated whole abdomen radiation therapy with regard to tolerance and efficacy in patients with carcinosarcomas of the uterus.

**Technical Approach:** Patients entering this study will have undergone surgical staging, TAH/BSO, and resection of gross intra-abdominal/pelvic disease. They will then be randomized to receive either radiation therapy (given as a hyperfractionated technique) or chemotherapy (utilizing ifosfamide with mesna and cisplatin). The chemotherapy will be administered over a four day period, at three week intervals. Patients treated with radiation therapy will receive twice a day treatments of 3000 cGy to the whole abdomen with a boost to the pelvis to 5000 cGy. Subsequent to therapy, patients will be seen in the clinic at three month intervals for two years and then six month intervals for the remainder of their follow-up, until completion of their analysis. Routine blood work evaluating renal and hepatic status will be obtained throughout therapy and in post-treatment follow-up.

**Progress:** No patients have been enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/134		<b>Status:</b> Completed	
<b>Title:</b> GOG 0151: Phase II Trial of Intraperitoneal Paclitaxel (Taxol) as Salvage Therapy in Patients with Small Volume Residual Ovarian Cancer Following Initial Systemic Chemotherapy					
<b>Start Date:</b> 08/05/94			<b>Est. Completion Date:</b> Jul 96		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Cancer:ovarian, paclitaxel, salvage therapy					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b>
					//

**Study Objective:** To evaluate the efficacy of Paclitaxel (Taxol) when administered intraperitoneally to patients with recurrent, small volume (< ml residual disease) ovarian disease.

**Technical Approach:** To be eligible for this study patients must have residual tumor nodules not in excess of 5 mm which were assessed at surgery. They will also have have either had a peritoneal catheter placed prior to entry or agree to have a catheter placed prior to treatment. Therapy will then be delivered by giving Paclitaxel (Taxol) at 60 mg/m<sup>2</sup> dissolved in 2 liters of normal saline through the peritoneal catheter on a weekly basis. Patients will be assessed hematologically on a weekly basis and a history and physical, routine liver function test, renal function test and tumor measurements will be obtained every four weeks. If tumor progression is noted therapy will be discontinued. If, at the completion of chemotherapy, imaging studies or physical examination does not demonstrate further evidence of disease the patient will undergo a reassessment operation to determine the response to therapy.

**Progress:** Study was closed to patient entry on 5 Sep 1995. No patients have been enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/150		<b>Status:</b> On-going	
<b>Title:</b> GOG 0152: A Phase III Randomized Study of Cisplatin & Taxol (Paclitaxel) With Interval Secondary Cytoreduction vs Cisplatin and Paclitaxel in Patients with Suboptimal Stage III & V....ovarian carcinom					
<b>Start Date:</b> 07/01/94			<b>Est. Completion Date:</b> Mar 96		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Cancer:ovarian, cisplatin paclitaxel, cytoreduction					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$23500.00		//	

**Study Objective:** To determine the impact of interval cytoreductive surgery on the progression free interval, survival and quality of life of patients with suboptimal debulked Stage III & IV epithelial ovarian cancer.

**Technical Approach:** All patients will have undergone maximal cytoreductive surgery for their cancer prior to entrance into the study. Subsequently, all patients will receive three treatments at three week intervals of Paclitaxel and Cisplatin by intravenous infusion. After three treatment cycles, patients will be re-evaluated to determine tumor response. Patients with stable disease or tumor response will then be randomized to secondary cytoreductive surgery followed by or three more courses of chemotherapy. Those receiving secondary cytoreductive surgery will receive three more courses of chemotherapy after surgery. Quality of life questionnaire will be completed at intervals during and after therapy.

**Progress:** No patients have been enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/149		<b>Status:</b> On-going	
<b>Title:</b> GOG 0153: A Phase II Study of Recurrent and "Advanced Endometrial Adenocarcinoma Treated With Alternating Courses of Megestrol Acetate (Megace) and Tamoxifen Citrate (Nolvadex)					
<b>Start Date:</b> 07/01/94			<b>Est. Completion Date:</b> Sep 95		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Cancer:endometrial, adenocarcinoma, megestrol acetate, tamoxifen					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		/ /	

**Study Objective:** To evaluate the potential up-regulating of progesterone receptors by Tamoxifen to enhance progesterone induced cell kill initiated by Megace therapy for recurrent or advanced endometrial carcinoma.

**Technical Approach:** Patients eligible for this study will be given megestrol acetate 160 mg/day x 3 weeks followed by tamoxifen citrate 40 mg/day for the next three weeks. This alternate sequence will continue until there is evidence of disease progression or grade 3 or 4 toxicity occurs. Patients will have a physical examination tynir measurements, documentation of major symptoms at six week intervals and HGB, HCT, CBC, Diff, and platelets will be determined every 3 months.

**Progress:** No patients have been enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/028		<b>Status:</b> On-going
<b>Title:</b> GOG 0154, Human Immunodeficiency Virus (HIV) Testing in Patients with Invasive Cervical Carcinoma.				
<b>Start Date:</b> 11/18/94		<b>Est. Completion Date:</b> JUL 98		
<b>Department:</b> GOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> Cervical Carcinoma				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//

**Study Objectives:** To determine the frequency of HIV infection in patients with all stages of epithelial cervical carcinoma. To evaluate the impact of HIV infection on the treatment and disease course in patients with cervical carcinoma.

**Technical Approach:** All patients who have invasive epithelial cervical cancers and who are less than 50 years of age will be eligible for participation. A list of total patients offered the protocol will be maintained without identifying factors along with those who agree to participate. Patients who agree will be counseled regarding the risks of HIV infection and will complete a questionnaire regarding additional risk factors. All patients who are HIV positive will continue to be followed in this study. They will be followed at six month intervals for one year, then yearly thereafter for the purposes of this study. A clinical summary form will be submitted at the completion of each visit. The GOG statistical Office will attempt match HIV positive patients with HIV negative patients based on age, tumor grade, stage and other potential confounding factors. Patients in both categories will be followed for disease progression or the development of secondary tumors as well as the occurrence of treatment related toxicity.

**Progress:** No patients have been enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/029		<b>Status:</b> On-going
<b>Title:</b> GOG 0155, Evaluation of Alpha-Interferon and Isotretinoin With or Without Zidovudine (AZT) in the Treatment of HIV-Infected Women with Invasive Cervical Carcinoma.				
<b>Start Date:</b> 11/18/94		<b>Est. Completion Date:</b> NOV 96		
<b>Department:</b> GOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> Cervical Cancer				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>
\$0.00		\$0.00		//

**Study Objectives:** To evaluate the anti-tumor affect and toxicity and toxicity profile of combination isotretinoin and alpha-interferon in HIV positive patients with cervical carcinoma.

**Technical Approach:** Patients with Bulky stage I and stages II-IV cervical cancer who are HIV positive are eligible for participation. Upon agreeing to participate, further treatment will be determined by the CD4 count. For patients with CD4 counts less than 500, treatment with daily interferon at 6 million units subcutaneously, daily isotretinoin at 1 mg/kg/d orally, and zidovudine (AZT) 100 mg five times per day orally will be initiated. At the end of a four week course, the patients will be re-evaluated. If significant progression of disease, as defined by greater than a 50% increase in tumor volume or the appearance of new lesions, patients will be discontinued for therapy and undergo standard oncologic therapy directed at their cervical cancer. Patients with CD4 counts greater than or equal to 500 will be treated similarly except they will not receive the zidovudine. Weekly CBC's, biweekly liver function tests and lipid profiles will be obtained. At four week intervals, CD4 counts and creatinine levels will also be obtained. After twelve weeks, patients will be evaluated for subsequent tumor-directed therapy. Patients will be followed at three month intervals for 2 1/2 years, at six month intervals for an additional three years and then every year.

**Progress:** No patients have been enrolled at MAMC.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/095		<b>Status:</b> On-going	
<b>Title:</b> GOG 0156: Randomized Trial of Pelvic Radiation versus Doxorubicin Plus Cisplatin in Stage IB, Stage IC, IIA, and IIB EnDometrial Carcinoma					
<b>Start Date:</b> 04/21/95			<b>Est. Completion Date:</b> Jun 00		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Cancer:endometrial, radiation, doxorubicin, cisplatin					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		/ /	

**Objective:** To compare radiation therapy versus chemotherapy in an adjuvant setting for high risk, early stage endometrial cancer.

**Approach:** Patients with high risk Stage IB, IC, IIA, or IIB endometrial cancer is defined in the patient eligibility Section 3.13, page 4 of the protocol will be randomized to receive either post operative radiation therapy or post operative chemotherapy. Radiation therapy will be given in standard pelvic fields to a total dose of 5040 cGy. Patients who are randomized to receive chemotherapy will receive Doxorubicin and Cisplatin therapy given at a dose of 60 mg/m<sup>2</sup> and 50 mg/m<sup>2</sup> respectively. Chemotherapy will be given at three week intervals for a total of six treatment cycles. While receiving therapy, patients randomized to radiation therapy will have weekly CBCs drawn and patients randomized to chemotherapy will have CBCs, liver function test, and creatine obtained immediately prior to the next cycle of chemotherapy. Subsequent to treatment, all patients will be followed at three to four month intervals for two years. Standard follow-up in the Gyn Oncology Clinic involves six month follow-up thereafter until five years from treatment. However, the protocol requires a less liberal follow-up of yearly evaluations after the two year anniversary date of therapy. Patients will be followed for evidence of progressive disease and survival.

**Progress:** No patients have been enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/096	<b>Status:</b> On-going
<b>Title:</b> GOG 0157: A Randomized Phase III Trial of Carboplatin (AUG 7.5) and Paclitaxel 175 mg/m <sup>2</sup> q 21 Days x 3 Courses versus the Same Regimen x 6 Courses in Patients With Selected Stage IC and II (A,B,C)...		
<b>Start Date:</b> 04/21/95	<b>Est. Completion Date:</b> May 01	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Mark E. Potter, MC		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> Cancer:ovarian, carboplatin, paclitaxel		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> / /

**Study Objective:** 1. To evaluate the role of Taxol in the treatment of early stage high risk epithelial ovarian cancers. 2. To determine the optimal number of treatment cycles for the treatment of high risk early stage epithelial ovarian cancer.

**Approach:** Patients entered into this study will be treated with intravenous Carboplatin at an area under the curve of 7.5. Taxol at 175 mg/m<sup>2</sup> will also be administered. Treatments will be provided intravenously at three week intervals. During the course of chemotherapy, weekly CBCs will be obtained to evaluate toxicity. Prior to each treatment cycle, a history and physical examination will be performed as well as creatine, CA-125 and urinalysis. Other investigative tests will be ordered as needed only. Patients will be randomized prior to the initiation of therapy to receive three or six cycles of chemotherapy. Dose reduction or the addition of G-CSF to reduce myelosuppressive side effects are outlined in the protocol. The primary modality to reduce toxicity will be dose reduction followed by the administration of G-CSF for repeated episodes or for febrile neutropenia. After the completion of therapy, patients will be followed in the GYN Oncology clinic on a monthly basis for six months and then every three months for four follow-up visits. Thereafter, they will be followed on a yearly basis for life.

**Progress:** No patients have been enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/072		<b>Status:</b> On-going	
<b>Title:</b> GOG 0158: A Phase III Randomized Study of A Platinum Compound and Paclitaxel in Optimal Stage III Epithelial Ovarian Carcinoma: Cisplatin vs Carboplatin and 3-Hour vs 96-Hour Infusions of Paclitaxel					
<b>Start Date:</b> 01/20/95			<b>Est. Completion Date:</b> Mar 98		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Cancer:ovary, cisplatin, carboplatin, paclitaxel, G-CSF					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$56222.00		/ /	

**Study Objective:** To compare the relative efficacy and toxicity of two different platinum compounds when utilized with taxol in two different infusions schemes for the treatment of patients with optimally debulked epithelial ovarian cancer.

**Approach:** Patients with optimally debulked Stage III epithelial ovarian cancer who agree to participate in this study will be randomized to four different treatment regimens. The treatment regimens will have two different variables (platinum compound selected - cisplatin or carboplatin and duration of infusion - 3 hours or 96 hours). All patients will be treated at three week intervals. Treatment will consist of six treatments followed by a second-look (reassessment laparotomy). Patients with progressive disease or obviously elevated CA-125's (> 100) will not be required to undergo a second-look laparotomy. After the completion of reassessment laparotomy, patients will be followed at monthly intervals for six months followed by three month intervals for additional 36 months and then every six months thereafter. Physical examinations and CA-125s will be obtained during follow-up.

**Progress:** No patients have been enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 90/026		<b>Status:</b> Completed	
<b>Title:</b> GOG 8907: DNA Content of Hydatidiform Moles as a Predictor of Persistent Gestational Trophoblastic Neoplasia					
<b>Start Date:</b> 01/19/90			<b>Est. Completion Date:</b> Indef.		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> trophoblastic neoplasia,DNA,hydatidiform moles					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		02/05/93	

**Study Objective:** To determine: if aneuploidy identifies a subset of high-risk hydatidiform moles; if ploidy status has sufficient predictive value to justify prophylactic chemotherapy of certain molar pregnancies; if proliferative activity, as estimated from cell cycle distribution, has any prognostic value; the number of paraffin blocks that constitutes an appropriate sampling of a molar pregnancy in order to establish presence of aneuploid cell lines; and if ploidy or proliferative index, as measured on either the mole or subsequent biopsy material, can predict the pattern of post-molar gestational trophoblastic neoplasia to be either metastatic or nonmetastatic and the response to various treatment regimens; and to assess persistence of ploidy status by comparing ploidy of molar tissue with ploidy status of subsequent tissue samples obtained after development of post-molar gestational trophoblastic disease.

**Technical Approach:** Flow cytometry will be used to measure ploidy and proliferative rate on archival tissues on patients identified as having complete hydatidiform mole pregnancies. These patients have previously been identified by entry on GOG Protocol #55. Results of lab measurements on tissue will be compared to clinical characteristics of post molar course, treatment received, if any, and response to such treatment. The incidence of aneuploidy in tissue samples from staging work-up in those patients who have developed persistent gestational trophoblastic neoplasia will be assessed. Information regarding cell cycle kinetics and growth fraction will be used to correlate tumor responses to treatment regimens in consideration of cell cycle phase specificity for various agents.

**Progress:** Study was closed to patient entry on 28 Jul 1994. No patients entered this study at MAMC.

### Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 95/030

**Status:** On-going

**Title:** GOG 9303, Cisplatin-DNA Adducts in Ovarian Cancer as a Predictor of Response to Platinum-based Chemotherapy.

**Start Date:** 11/18/94

**Est. Completion Date:** MAR 96

**Department:** GOG

**Facility:** MAMC

**Principal Investigator:** LTC Mark E. Potter, MC

**Associate Investigators:** None

**Key Words:** Ovarian Cancer

**Accumulative**

**Est. Accumulative**

**Periodic Review:**

**MEDCASE Cost:** \$0.00

**OMA Cost:** \$0.00

//

**Study Objectives:** To determine if the level of Platinum-DNA adducts predict responsiveness to the chemotherapeutic regimen of Taxol-Cisplatin in advanced ovarian cancer.

**Technical Approach:** This investigation is a companion protocol to GOG 152, which investigates the utilization of interval cytoreduction in patients treated with cisplatin and taxol for bulky advanced ovarian cancer. Only patients who are entered in to protocol GOG 152 are eligible for participation in this protocol. Consequently, there are no additional risks for surgery or chemotherapy from participation in this protocol. Subjects will have 40-50 cc of blood drawn 24 hours after administration of the first dose of cisplatin. No additional blood or tissue samples will be obtained. All information regarding tumor response and patient survival will already be provided and available as per protocol 152. The blood levels of DNA products will be analyzed with regard to the response to chemotherapy and overall patient survival.

**Progress:** No patients have been enrolled at MAMC.

**DETAIL SHEETS FOR PROTOCOLS**

**NATIONAL SURGICAL ADJUVANT BREAST & BOWEL  
PROJECT**

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 93/147	<b>Status:</b> On-going
<b>Title:</b> NSABP R-03: A Clinical Trial to Evaluate the Worth of Preoperative Multimodality Therapy (5-FU-LV and RTX) in Patients with Operable Carcinoma of the Rectum		
<b>Start Date:</b> 08/06/93	<b>Est. Completion Date:</b> Jul 98	
<b>Department:</b> NSABP	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Timothy P. Rearden, MC		
<b>Associate Investigators:</b>		LTC Luke M. Stapleton, MC
LTC Howard Davidson, MC		MAJ Kenneth A. Bertram, MC
MAJ Patrick L. Gomez, MC		MAJ Mark E. Robson, MC
MAJ Robert B. Ellis, MC		MAJ Richard C. Tenglin, MC
CPT James S. D. Hu, MC		LTC Robert D. Vallion, MC
CPT Diana S. Willadsen, MC		CPT John R. Caton, MC
<b>Key Words:</b> cancer:rectum, 5-FU, leucovorin, radiotherapy		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	12/17/93

**Study Objective:** 1). To determine whether the administration of chemotherapy (5-FU-LV with radiotherapy preoperatively is more effective than the administration of the chemotherapy and radiotherapy postoperatively in improving disease-free survival and survival in patients with operable carcinoma of the rectum. 2). To determine if the administration of the above chemotherapy and radiotherapy preoperatively results in improvement local recurrence rates when compared with the regimen administered postoperatively in this population of patients. 3). To evaluate the response of rectal tumors to preoperative chemotherapy and radiotherapy and to correlate that response with disease-free survival and survival. 4). To assess the downstaging effect of preoperative chemotherapy and radiotherapy on the tumor size and the pathologic status of regional lymph nodes. 5). To estimate the proportion of patients who can be converted to sphincter-saving surgical procedures from abdominoperineal resection. Furthermore, to estimate the proportion of patients who can be converted from sphincter-saving surgical procedures to local excision alone.

**Technical Approach:** This trial in patients with operable adenocarcinoma of the rectum compares the worth of seven cycles of 5-FU (FU) + leucovorin (LV) and radiotherapy (RTX), where the first three cycles are given preoperatively and the remaining four postoperatively, to seven cycles of FU-LV and RTX given postoperatively. The patients will be randomized into 2 groups. Group 1 patients, in cycle 1, will receive LV 500 mg/m<sup>2</sup> by IV infusion and FU 500 mg/m<sup>2</sup> will be started 1 hr later. Treatment will be given weekly for 6 weeks followed by a rest period. Treatment will be restarted 21 days after the date of administration of the sixth dose of the previous cycle. Radiotherapy will begin after completion of cycle 1. FU 325 mg/m<sup>2</sup>/day and LV 20 mg/m<sup>2</sup>/day will be given for 5 days during the first and fifth weeks of radiotherapy (cycles 2 and 3). Surgery will be performed after completion of the radiation therapy. After recovery from surgery, four more cycles of FU with LV, as in cycle 1, will be given for a total of seven cycles. Groups 2 patients should have surgery performed no later than 3 weeks after randomization. Chemotherapy will begin after recovery from surgery is complete but no later than 4 weeks postoperatively. LV and FU will be administered as in Group 1. Radiotherapy will begin after completion of cycle 1. Cycle 4 should begin after completion of radiotherapy when counts allow, but no later than 5 weeks. Four more cycles of FU with LV will be given for a total of seven cycles. The primary endpoints are diseases free survival and survival.

**Progress:** No patients have yet been enrolled.

**DETAIL SHEETS FOR PROTOCOLS**

**PEDIATRIC ONCOLOGY GROUP**



### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/141		<b>Status:</b> On-going
<b>Title:</b> POG 8650: Intergroup National Wilms' Tumor Study - 4				
<b>Start Date:</b> 06/09/93		<b>Est. Completion Date:</b> Oct 97		
<b>Department:</b> POG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Shirley E. Reddoch, MC				
<b>Associate Investigators:</b> COL Bruce A. Cook, MC		MAJ Stephen R. Palmer, MC		
<b>Key Words:</b> cancer:pediatric, Wilms'				
<b>Accumulative</b> <b>MEDCASE Cost:</b> \$0.00		<b>Est. Accumulative</b> <b>OMA Cost:</b> \$0.00		<b>Periodic Review:</b> 04/21/95

**Study Objective:** To compare 1) the relapse-free and overall survival percentages of patients with: Stage I and II favorable histology (FH) and Stage I anaplastic Wilms' tumor (Ana), using conventional versus pulse intensive (P/I) chemotherapy with vincristine and actinomycin D; (2) Stages 3 and 4 FH, and Stages 1-4 clear cell sarcoma of the kidney using conventional versus P/I vincristine, actinomycin D, and Adriamycin plus radiation therapy; (3) Stages 2-4 Ana treated with vincristine, actinomycin D, and Adriamycin versus the same 3 drugs plus cyclophosphamide, and radiation therapy; and (4) Stages 2-4 FH and Stage 1-4 clear cell sarcoma of the kidney treated for 6 versus 14 months after nephrectomy.

**Technical Approach:** All patients will be <16 years of age, have had no prior chemo-radiation therapy, will have undergone nephrectomy, and will meet other criteria as stated in the protocol. Patients will be randomized as follows: Stage II/FH & Stage I Ana receive A + V (24 wks) or P/I A + V (18 wks), Stage II/FH receive A + V (22 vs 65 wks) or P/I A + V (60 wks), Stages III & IV FH & clear cell (I-IV) receive A + V + D (26 vs 65 wks) plus RT or P/I A + V + D (24 vs 54 wks) plus RT, and Stages II-IV Ana receive A + V + D + C (65 wks) plus RT or A + V + D + C (65 wks) plus RT. Legend: A = actinomycin D, V = vincristine, D = doxorubicin (Adriamycin), C = cyclophosphamide, and RT = radiation therapy.

**Progress:** This protocol was closed to patient entry, 1 Sep 94. One patient enrolled at MAMC in FY93 is being followed.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/052		<b>Status:</b> On-going	
<b>Title:</b> POG 8930: A Comprehensive Genetic Analysis of Brain Tumors					
<b>Start Date:</b> 12/16/94			<b>Est. Completion Date:</b> Nov 97		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Shirley E. Reddoch, MC					
<b>Associate Investigators:</b> COL Bruce A. Cook, MC			MAJ Stephen R. Palmer, MC		
<b>Key Words:</b> Cancer:brain, genetics					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		/ /	

**Study Objective:** 1) To determine prospectively the clinical significance of abnormalities of cellular DNA content, as measured by flow cytometry in pediatric brain tumors. 2) To determine the clinical implications of cytogenetic abnormalities found in pediatric brain tumors at diagnosis. 3) To determine the clinical significance of amplification or rearrangement of specific cellular proto-oncogenes or allelic loss of recessively-acting loci in DNA extracted from pediatric brain tumors. 4) To attempt to derive tumor cell lines and to provide a bank of frozen brain tumor tissue for use in further studies, especially molecular genetic studies.

**Approach:** This is a non-therapeutic study intended to prospectively collect tissue from newly diagnosed patients with brain tumors. Flow cytometry, cytogenetics, and molecular studies will be used to characterize abnormalities of the DNA and correlate their findings with type of disease/diagnoses, tumor grade, and prognostic indicators.

**Progress :** No patients have been enrolled in this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/039		<b>Status:</b> Completed	
<b>Title:</b> POG 9000: ALinC #15 Lab Classification Protocol					
<b>Start Date:</b> 11/18/94			<b>Est. Completion Date:</b> Dec 94		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL Bruce A. Cook, MC					
<b>Associate Investigators:</b>			MAJ Stephen R. Palmer, MC		
<b>Key Words:</b> leukemia:pediatric, laboratory classification					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		/ /	

**Study Objectives:** 1) To continue the characterization of the biologic findings of acute lymphoblastic and undifferentiated leukemias and their relationship, as prognostic factors for attaining and maintaining remission. 2) To apply to therapy selection, the determinatin that ploidy and certain structural chromosomal abnormalites predict poor progneosis. 3) To determine if outcome is related to patient differences in methotrexate (MTX) availability. 4) To determine the frequency of myeloperoxidase (MPO) gene espression in the blast cell population of all newly diagnosed cases of infant leukemia. 5) To determine by *in vitro* testing if there is inadvertant stimulation of infants' lymphoblasts by hematopoietic grwoth factors (HGF). 6) To evaluate the usefulness of the Polymerase Chain Reaction (PCR) technique in detecting minimal residual disease in patients with disease demonstrating t(9;22) or t(1;19) chromosomal abnormalities.

**Technical Approach:** This study involves performing the evaluations listed above on bone marrow aspirates collected from patients with acute lymphoblastic and undifferentiated leukemias. At the time of diagnostic evaluation, which includes bone marrow aspiration and/or biopsy, 10-13 ml of bone marrow will be collected and divided for preparation and distribution to the centers involved. Corresponding periperal blood and bone marrow slide would be provided to the centers as required and to the University of Mississippi for slide bank. If marrow is inaspiratable and/or peripheral blood WBC count is >30,000 with >75% blasts, peripheral blood could be substituted for bone marrow. At the time of follow up bone marrow evaluation, bone marrow sample would be provided to Standford for PCR analysis if a t(9;22) or t(1;19) chromosomal positive acute lyphoblastic leukemia has been identified.

**Progress :** This study closed to patient accrual 15 Sept 94. No patients were enrolled in this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/018		<b>Status:</b> On-going	
<b>Title:</b> POG 9031: Treatment of Children with High Stage Medulloblastoma: Cisplatin/VP-16 Pre vs Post-Irradiation					
<b>Start Date:</b> 11/18/94			<b>Est. Completion Date:</b> Nov 94		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Shirley E. Reddoch, MC					
<b>Associate Investigators:</b> COL Bruce A. Cook, MC			MAJ Stephen R. Palmer, MC		
<b>Key Words:</b> Pediatric Cancer:medulloblastoma, cisplatin, VP-16, radiation					
<b>Accumulative</b> <b>MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative</b> <b>OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> / /

**Study Objectives:** To compare the 2-year event-free survival (EFS) of children with newly-diagnosed high-risk medulloblastoma who are treated with cisplatin and VP-16 pre-irradiation vs post-irradiation. To define the toxicity and activity of pre-irradiation cisplatin/VP-16 in patients with newly-diagnosed high-risk medulloblastoma. To determine whether achievement of a measurable tumor response (PR and CR) to pre-irradiation cisplatin/VP-16 has prognostic significance for children with high-risk medulloblastoma, compared with failure to achieve a measurable response (SD or PD). To define the toxicity and activity of post-irradiation cisplatin/VP-16 in patients with newly-diagnosed high-risk medulloblastoma. To determine if c-myc amplification in medulloblastoma is associated with an adverse prognosis.

**Technical Approach:** Studies in children and adults have demonstrated the ability to deliver pre-radiotherapy chemotherapy for patients with newly-diagnosed brain tumors without increasing neurotoxicity in association with the subsequent radiotherapy. This approach creates a phase II "window" allowing evaluation of response in these patients who are previously untreated except for surgery. The theoretical anti-neoplastic advantage of this approach is the potentially enhanced efficacy of the radiotherapy when given to "chemically debulked" patients. Half of the children diagnosed with medulloblastoma are now being successfully treated and are surviving for prolonged periods. Until recently, the survival of this group of patients was limited so that long-term effects of therapy were not a concern. As survival increases, one would expect to observe an increase in frequency of certain treatment-related toxicities. There are now a variety of long-term effects which need to be considered in this cohort of patients. Specific evaluations will be made on all patients entered onto this study, so that treatment-related problems may be detected in their early stages and intervention taken. This approach should ultimately improve the quality of life for children diagnosed and treated for brain tumors.

**Progress :** One patient was enrolled in this study at MAMC in FY95 and continues to be followed.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/164		<b>Status:</b> On-going	
<b>Title:</b> POG 9047: Neuroblastoma Biology Protocol					
<b>Start Date:</b> 09/03/93			<b>Est. Completion Date:</b> Feb 96		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Shirley E. Reddoch, MC					
<b>Associate Investigators:</b> MAJ Stephen R. Palmer, MC			COL Stephen R. Stephenson, MC COL Bruce A. Cook, MC		
<b>Key Words:</b> cancer:neuroblastoma, biology					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	04/21/95	

**Study Objective:** 1) To obtain tissue for the analysis of DNA content of neuroblastoma cells by flow cytometry. 2) To characterize neuroblastoma tumor DNA from POG patients genetically by analysis of N-myc amplification and LOH for chromosome 1p. 3) To develop a reference bank of genetically characterized tumor tissue and DNA that would be available for other studies.

**Technical Approach:** This is a non-therapeutic study intended to collect tissue from newly-diagnosed neuroblastoma patients  $\leq 21$  years. Viable tumor tissue, frozen tumor tissue (or marrow) and serum will be collected and forwarded to a designated study site.

**Progress:** No patients have been enrolled in this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/017		<b>Status:</b> On-going	
<b>Title:</b> POG 9135: Pre-radiation Chemotherapy for Children with Supratentorial Malignant Gliomas and Poorly Differentiated Embryonal Tumors					
<b>Start Date:</b> 11/18/94			<b>Est. Completion Date:</b> Jun 97		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Shirley E. Reddoch, MC					
<b>Associate Investigators:</b> COL Bruce A. Cook, MC			MAJ Stephen R. Palmer, MC		
<b>Key Words:</b> Cancer: glioma, Cancer:embryonal, radiation, chemotherapy					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> / /

**Study Objectives:** To estimate the response of children with supratentorial malignant glioma or poorly-differentiated embryonal tumors (PDET)s to three cycles of either BCNU plus continuous-infusion cisplatin or cyclophosphamide plus continuous-infusion etoposide (VP-16). To determine the acute and sub-acute toxicities of these combination chemotherapies. To estimate prospectively, using neuroimaging studies and CSF cytology, the incidence of neuraxis tumor dissemination at diagnosis in children with measurable residual tumor following initial surgery.

**Technical Approach:** Patients will be randomized and begin chemotherapy within 4 weeks of diagnostic surgery. One patient per year is expected from MAMC for this study and will be randomized to either Treatment A or Treatment B. Patients will be off study after completion of three courses of chemotherapy or upon unequivocal evidence of progressive disease. They will then register on POG 9136 for radiation therapy.

**Progress :** No patients have been enrolled in this study at MAMC.

## Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 95/015

**Status:** On-going

**Title:** POG 9150/CCSG 6901 - Intergroup Rhabdomyosarcoma Study-IV for Stage I Disease.

**Start Date:** 11/18/94

**Est. Completion Date:** JUN 97

**Department:** POG

**Facility:** MAMC

**Principal Investigator:** LTC Shirley E. Reddoch, MC

**Associate Investigators:**  
COL Bruce A. Cook, MC

MAJ Stephen R. Palmer, MC

**Key Words:** Rhabdomyosarcoma

**Accumulative**

**Est. Accumulative**

**Periodic Review:**

**MEDCASE Cost:** \$0.00

**OMA Cost:** \$0.00

//

**Study Objectives:** To compare the progression-free survival rates of patients receiving vincristine-actinomycin-D-cytosine (VAC) vs patients receiving vincristine-actinomycin-D-ifosfamide (VAI) vs those receiving vincristine-ifosfamide-etoposide (VIE) for treatment of rhabdomyosarcoma and undifferentiated sarcoma. To compare hyperfractionated radiation therapy (RT) to conventional RT in regard to: a) local relapse rates, and b) early/acute toxicity and late effects. To investigate the relationship between immunohistochemical pattern of tumor and prognosis, and to evaluate newly identified immunohistochemical markers in diagnosis. To correlate clinical features of disease and prognosis with tumor cytogenetics, DNA index and amplification or rearrangement of specific cellular proto-oncogenes. To provide a bank of frozen tumor tissue for use in tumor biology studies. To evaluate the use of recombinant G-CSF as a supportive measure for ameliorating hematopoietic toxicity.

**Technical Approach:** This is a randomized 3-arm study with an internal control consisting of a modified repetitive pulse VAC regimen for Stage 1 disease, excluding Clinical Group I paratesticular and Groups I and II orbit/eyelid patients, in IRS-IV. The modifications of VAC involve maximizing its intensity: cytosine is delivered in a single high dose rather than at a lower dose daily x 3, actinomycin-D is delivered more frequently in induction, and VCR more frequently during continuation. The two experimental arms differ from the control in that ifosfamide is substituted for cytosine in one (VAI) and ifosfamide + VP-16 are substituted for actinomycin-D + cytosine in the other (VIE). The comparison then, is VAC vs VAI vs VIE. Clinical Group I paratesticular and orbit/eyelid patients will be treated separately with VA alone. The second major comparison and randomization in IRS-IV will be between conventional RT and hyperfractionated RT (Hyperfx-RT) in stages 1, 2, and 3 patients with gross residual disease after surgery (clinical group III). Within each stage, except for stage 4 radiotherapy will be randomized or assigned by Clinical Group. Participation in the corresponding tumor study (PO #9153) is required.

**Progress :** No patients have been enrolled in this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/016		<b>Status:</b> On-going	
<b>Title:</b> POG 9151/CCSG 6902 - Intergroup Rhabdomyosarcoma Study-IV for Stage II and Stage III Diseases.					
<b>Start Date:</b> 11/18/94			<b>Est. Completion Date:</b> JUN 97		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Shirley E. Reddoch, MC					
<b>Associate Investigators:</b> COL Bruce A. Cook, MC			MAJ Stephen R. Palmer, MC		
<b>Key Words:</b> Rhabdomyosarcoma					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		/ /	

**Study Objectives:** To compare the progression-free survival rates of patients receiving vincristine-actinomycin-D-cytosine (VAC) vs patients receiving vincristine-actinomycin-D-ifosfamide (VAI) vs those receiving vincristine-ifosfamide-etoposide (VIE) for treatment of rhabdomyosarcoma and undifferentiated sarcoma. To compare hyperfractionated radiation therapy (RT) to conventional RT in regard to a) local relapse rates, and b) early/acute toxicity and late effects. To investigate the relationship between immunohistochemical pattern of tumor and prognosis, and to evaluate newly identified immunohistochemical markers in diagnosis. To correlate clinical features of disease and prognosis with tumor cytogenetics, DNA index and amplification or rearrangement of specific cellular proto-oncogenes. To provide a bank of frozen tumor tissue for use in tumor biology studies. To evaluate the use of recombinant G-CSF as a supportive measure for ameliorating hematopoietic toxicity.

**Technical Approach:** This study is designed to determine whether an ifosfamide-based combination (VAI) is superior to a cyclophosphamide-based combination (VAC) in previously untreated patients. Therefore, a randomized 3-arm study with an internal control consisting of a modified repetitive pulse VAC regimen is the study to be undertaken for stages 2 and 3 disease in IRS-IV. The two experimental arms (VAI and VIE) differ from the control arm as follows: ifosfamide is substituted for cyclophosphamide in one cyclophosphamide in the other (VIE). The comparison then, is VAC vs VAI vs VIE in IRS-IV. The second major comparison and randomization in IRS-IV will be between conventional RT and hyperfractionated RT (Hyperfx-RT) in stages 1, 2 and 3 patients with gross residual disease after surgery (clinical group III). The goal is to try to improve the local control rate in these Group III patients with Hyperfx-RT, whereas Group II patients in these stages have an acceptable local control rate of 90% with conventional RT and will continue to receive conventional RT in IRS-IV.

**Progress :** No patients have been enrolled in this study at MAMC.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/007		<b>Status:</b> Completed
<b>Title:</b> POG 9152: Intergroup Rhabdomyosarcoma Study-IV for Stage 4 and/or Clinical Group IV Diseases, All Patients with Metastasis.				
<b>Start Date:</b> 11/04/94		<b>Est. Completion Date:</b> JUN 97		
<b>Department:</b> POG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL Bruce A. Cook, MC				
<b>Associate Investigators:</b>		MAJ Stephen R. Palmer, MC		
<b>Key Words:</b> Rhabdomyosarcoma				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>
\$0.00		\$0.00		//

**Study Objective:** 1) To rank order three treatment strategies according to progression-free survival and overall survival rates for rhabdomyosarcoma and undifferentiated sarcoma, 2) to determine whether there is clinical cross-resistance between the drug pairs used upfront and subsequent vincristine, actinomycin-D, cyclophosphamide therapy in patients who achieve less than a Clinical Response to the induction doublets, 3) to investigate the relationship between immunohistochemical pattern of tumor and prognosis, and to evaluate newly identified immunohistochemical markers in diagnosis, 4) to correlate clinical features of disease and prognosis with tumor cytogenetics, DNA index and amplification or rearrangement of specific cellular proto-oncogenes, 5) to provide a bank of frozen tumor tissue for use in tumor biology studies and 6) to evaluate the use of recombinant G-CSF as a supportive measure for ameliorating hematopoietic toxicity.

**Technical Approach:** Patients will be randomized to either Regimen 48 induction with Vincristine IV (1.5 mg/M<sup>2</sup> q wk x 6) plus Melphalan IV (30 mg/M<sup>2</sup> weeks 1 and 5); or Regimen 49 induction with VP-16 IV (100 mg/M<sup>2</sup>/day x 5 days weeks 1 & 4, starting day 0) plus Ifosfamide IV (1.8 gm/M<sup>2</sup>/day x 5 days, weeks 1 & 4, starting day 0) and MESNA IV (360 mg/M<sup>2</sup> given 15 minutes before the ifosfamide and then q 3 hours IV or PO after each ifosfamide dose. G-CSF will be given (5 ug/kg/day s.c. until ANC is >1000/ul, starting 24 to 48 hours after each combination chemotherapy course or melphalan alone.

Patients will be evaluated for response following week 6 of induction therapy and continued on induction if a clinical response (CR), partial response (PR) or Objective Improvement is noted.

Patients showing no response (NR) or progressive disease (PD) following the 6 weeks of induction therapy will go on to week 13 (begin drug regimens of week 13-18 in week 7) and then for continuation therapy (week 25 onward) give only vincristine, actinomycin-D, and cyclophosphamide. Radiotherapy will begin at week 18.5 to the tumor bed and sites of metastasis.

**Progress :** This study was closed to patient accrual 1 Mar 95. No patients were enrolled in this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/008		<b>Status:</b> On-going	
<b>Title:</b> POG 9153: Intergroup Rhabdomyosarcoma Study/Laboratory Evaluation of Tumor Tissue					
<b>Start Date:</b> 11/04/94			<b>Est. Completion Date:</b> JUN 97		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Shirley E. Reddoch, MC					
<b>Associate Investigators:</b> COL Bruce A. Cook, MC			MAJ Stephen R. Palmer, MC		
<b>Key Words:</b> Rhabdomyosarcoma					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		//

**Study Objective:** 1) To prospectively correlate clinical features and outcome of newly diagnosed children with rhabdomyosarcoma with cytogenetic abnormalities of their tumors, 2) to measure cellular DNA content by flow cytometry of tumor cells and correlate the DNA index of tumor stem lines with clinical features and treatment response, 3) to determine prospectively the clinical significance of amplification or rearrangement of specific cellular proto-oncogenes or allelic loss of recessively acting loci in DNA extrated from pediatric rhamdomyosarcomas, 4) to attempt to derive tumor cell lines and to provide a bank of frozen rhabdomyosarcoma tumor tissue for use in further studies, especially molecular genetic studies, and 5) to determine the degree of specificity of monoclonal antibody probes, 4.2A8, 5.1H11, and 3.1G11, for childhood rhabdomyosarcoma.

**Technical Approach:** This is a non-therapeutic study intended to collect tissue from newly-diagnosed rhabdomyosarcoma and undifferentiated sarcoma patients  $\leq 21$  years. Viable tumor tissue, frozen tumor tissue and involved marrow samples will be collected and forwarded to a designated study site.

**Progress :** No patients have been enrolled in this study at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/084		<b>Status:</b> On-going	
<b>Title:</b> POG 9182: HIV/Malignancy Biology Protocol					
<b>Start Date:</b> 03/17/95			<b>Est. Completion Date:</b> Apr 97		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Shirley E. Reddoch, MC					
<b>Associate Investigators:</b> COL Bruce A. Cook, MC			MAJ Stephen R. Palmer, MC		
<b>Key Words:</b> Cancer:lymphoma, HIV					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		/ /	

**Study Objective:** 1) To establish a national registry of pediatric AIDS-associated lymphomas and other malignancies and a repository of well-characterized tumor tissue, cells and sera from affected patients. 2) To conduct prospective Phase I-III clinical trials of anti-cancer and anti-retroviral therapies aimed at improving outcomes and identifying critical determinants of risk. 3) To identify the presence and quantify the viral burden of human immunodeficiency virus (HIV), Epstein-Barr virus (EBV), cytomegalovirus (CMV), Human Herpes virus 6 (HHV6), and Herpes Simplex virus (HSV) in the tumor tissue, peripheral blood cells, plasma, and cerebrospinal fluid of pediatric patients with lymphomas and other malignancies; and to characterize the effect of anti-cancer and antiviral chemotherapy with regard to lymphoma stage, disease progression, host response, and toxicity. 4) To conduct the first large-scale molecular epidemiologic study of risk factors related to development of HIV-related NHL in children by means of a case-control analysis of HIV-infection characteristics such as co-infection with EBV, CMV, HHV6, Mycoplasma, the quantitative host viral burden, level of immunodeficiency, and other host characteristics. 5) For HIV+ and HIV- children, to characterize differences in NHL tumor tissue in terms of immunophenotype, immunoglobulin gene rearrangements and oncogene (c-myc) activation.

**Approach:** Three groups of children are eligible for this protocol. The first, a "case" group, consists of children with a newly-diagnosed malignancy who are HIV positive. The second, a "malignancy control" group, consists of children with a newly-diagnosed malignancy who do NOT have HIV infection. The third group, a "non-malignancy control" group, consists of children with no evidence of malignancy, but who have a documented HIV infection. A total of 150, 150, and 300 patients, respectively is expected. The subject will be seen in the clinic at least every two months for up to two years, then every 6 months up to 3 years. At each visit blood will be drawn for testing. In addition, a small piece of tumor tissue or other body fluids (including spinal fluid and bone marrow), already obtained as part of routine clinical management may be examined. We will establish a database as a repository for characteristics of pediatric patients with HIV infection and malignancies. The database will include all appropriate clinical parameters, laboratory measures, and results of molecular and virologic studies. Descriptive analyses of clinical and laboratory data will use various criteria to characterize the study population and to correlate variation in infectious virus and total viral burden with clinical course and other laboratory measurements. Primary endpoints, which may include tumor response, disease-free survival and episodes of grade 3-4 toxicities, will be confined to those specified in POG therapeutic protocols. Contingency tables relating the laboratory variables with stage, age, primary tumor site, histopathology, and clinical response will be produced. Conditional

logistic regression will be used to compare biological data for cases to matched controls. Frequency matching will be performed at the Statistics Office at the time of analysis. Kaplan-Meier life tables, log rank tests, and Cox regression will be used to explore the relationship of laboratory variables to outcome.

Progress : No patients have been enrolled in this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/056		<b>Status:</b> On-going	
<b>Title:</b> POG 9201: ALINC #16 Treatment for Patients with Lesser Risk Acute Lymphoblastic Leukemia, A Pediatric Oncology Group Phase III Study					
<b>Start Date:</b> 12/16/94			<b>Est. Completion Date:</b> Dec 99		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Shirley E. Reddoch, MC					
<b>Associate Investigators:</b> COL Bruce A. Cook, MC			MAJ Stephen R. Palmer, MC		
<b>Key Words:</b> leukemia:pediatric, leukemia:lymphoblastic, cytosine arabinoside, leucovorin calcium, hydrocortisone, 6-Mercaptopurine, methotrexate, E. coli asparaginase, Erwinia asparaginase, prednisone, vincristine					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		/ /	

**Study Objective:** 1) To confirm the outstanding results in patients with lesser risk not-T, non-B acute lymphoblastic leukemia (ALL) treated in a fashion similar to the least intensive arm of POG 8602 (AlinC 14, Arm A). 2) To study laboratory correlates from POG 9400 and clinical correlates with outcome in pooling studies 9201, 9405, and 9406.

**Approach:** Patients on this study will be treated with a 3-drug induction regimen (vincristine, prednisone, and L-asparaginase) to bring about remission (a state of no apparent disease) in four weeks.

This will be followed by a consolidation phase including (6) six courses of intravenous (into vein) intermediate-dose methotrexate (each will require hospital stay) at 3-week intervals. After week 5, daily 6-mercaptopurine will be given by mouth until the end of planned treatment. Methotrexate will be given intramuscularly (into muscle) weekly. Periodic "pulses" (infrequent administration) of vincristine and prednisone will be given throughout the first two years of therapy. Additionally, triple intrathecal (into spinal fluid) therapy (TIT) consisting of methotrexate, hydrocortisone, cytosine arabinoside will be given at the start of treatment and periodically through the first two years of therapy to prevent the spread of leukemia to the central nervous system (CNS). The vitamin Leucovorin will be given to prevent methotrexate toxicity. After week 25, during the continuation phase, all medications will be on an outpatient basis.

The total duration of therapy is planned to be 2 1/2 years from initial diagnosis. If tests at that time indicate no evidence of leukemia, then all medications will be stopped and you (your child) will be followed closely to be sure that there is no evidence of return of the disease.

**Progress :** No patients have been enrolled in this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/033		<b>Status:</b> On-going	
<b>Title:</b> POG 9219: Treatment of Localized Non-Hodgkin's Lymphoma, A POG Phase IV Study					
<b>Start Date:</b> 11/05/93			<b>Est. Completion Date:</b> Jun 96		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Shirley E. Reddoch, MC					
<b>Associate Investigators:</b> MAJ Stephen R. Palmer, MC			COL Stephen R. Stephenson, MC COL Bruce A. Cook, MC		
<b>Key Words:</b> Cancer:non-Hodgkin's, cyclophosphamide, adriamycin, prednisone, methotrexate, 6-mercaptopurine, ARA-C, hydrocortisone					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	04/21/95	

**Study Objective:** 1. To maintain a high cure rate with minimum toxicity for children with localized non-Hodgkin's lymphoma in favorable sites. 2. To analyze in a large group of patients with localized non-Hodgkin's lymphoma (by pooling data from POG #83314, #8719 and the current study) prognostic factors which may predict subgroups of patients with a poor prognosis within the subgroup of patients with localized NHL.

**Technical Approach:** After staging, subjects that qualify will receive Vincristine 1.5 mg/m<sup>2</sup> (max 2 mg) IV q wk x 6 weeks, prednisone 40 mg/m<sup>2</sup>/day in 3 divided doses x 28 days, Adriamycin 40 mg/m<sup>2</sup>/day IV days 1 & 22, and Cyclophosphamide 750 mg/m<sup>2</sup>/day IV days 1 & 22. Fluid intake is to be > 3000 ml/m<sup>2</sup> on day of treatment. Triple intrathecal chemotherapy (TIT) will be given on days 1, 8, and 22 to those with head and neck primaries. On day 43, or when blood counts recover, the patient will receive Adriamycin 40 mg/m<sup>2</sup> IV, Cyclophosphamide 750 mg/m<sup>2</sup> IV, Vincristine 1.5 mg/m<sup>2</sup> (max 2 mg) IV, and Prednisone 50 mg/m<sup>2</sup> in 3 divided doses x 5 days. On day 64 and when blood counts have returned to normal following the prescribed induction and consolidation regimen, the patient will be assessed for remission status.

**Progress:** No patients have been enrolled in this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/147	<b>Status:</b> Completed
<b>Title:</b> POG 9220: Phase II Randomized Study of All-Trans Retinoic Acid Versus Cytosine Arabinoside and Daunorubicin as Induction Therapy for Patients With Previously Untreated Acute Promyelocytic Leukemia		
<b>Start Date:</b> 07/01/94	<b>Est. Completion Date:</b> Jul 96	
<b>Department:</b> POG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Shirley E. Reddoch, MC		
<b>Associate Investigators:</b> COL Bruce A. Cook, MC                      MAJ Stephen R. Palmer, MC		
<b>Key Words:</b> Cancer:leukemia, Cancer:children, all-trans retinoic acid, ARA-C, daunorubicin		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objective:** 1) To compare the complete remission rate and disease-free survival of TRA to that achieved with conventional induction chemotherapy including Cytosine Arabinoside plus Naunorubicin in patients with previously untreated APL. 2) To compare the toxicities of TRA to those of Cytosine Arabinoside plus Naunorubicin as induction therapy in APL. 3) To determine the value of maintenance therapy with TRA.;

**Technical Approach:** This study involves two randomizations. Patients will be initially randomized to either TRA or Daunorubicin plus Cytosine Arabinoside as induction therapy. Consistent with other ECOG studies, 1 or 2 cycles of Daunorubicin plus Cytosine Arabinoside will be permitted to achieve CR since approximately 20% of patients not achieving CR with 1 cycle do so with a second cycle. Following 2 cycles of consolidation chemotherapy for patients achieving CR, patients will be randomized (second randomization) to either maintenance TRA or observation until relapse. Ancillary laboratory studies will explore biological correlations of TRA responsiveness, and the pathophysiology of the coagulopathy.

**Progress:** This study was closed to patient accrual 13 Feb 95. No patients were enrolled in this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/148		<b>Status:</b> On-going
<b>Title:</b> POG 9233/34: A Phase III Randomized Trial of standard vs Dose-Intesntified Chemotherapy for Children Less Than 3 Years of Age With A CNS Malignancy Treated With or Without Radiation Therapy				
<b>Start Date:</b> 08/06/93		<b>Est. Completion Date:</b> Jun 95		
<b>Department:</b> POG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Shirley E. Reddoch, MC				
<b>Associate Investigators:</b> MAJ Stephen R. Palmer, MC		COL Stephen R. Stephenson, MC COL Bruce A. Cook, MC		
<b>Key Words:</b> cancer:CNS, pediatric, chemotherapy, radiotherapy				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>
\$0.00		\$0.00		02/04/94

**Study Objective:** To develop effective methods of treatment for very young children with malignant brain tumors that will minimize late toxicities affecting immature and rapidly developing central nervous systems.

**Technical Approach:** Patients < 3 yrs of age with a primary intracranial malignancy will be randomized to one of two regimens. Patients assigned to Regimen A will receive six 12-week courses of chemotherapy, given over a total of 72 weeks. Each course consist of 3 drug cycles. Cycle A; vincristine and cyclophosphamide and Mesna will be given on weeks 1, 13, 25, 37, 49 and 61. Vincristine will be repeated on day 8 of this cycle. During Cycle B, patients will receive cisplatin on day 1 and VP-16 on days 3 and 4. Patients on Regimen B will receive eight 9-week courses of chemotherapy. Each course will consist of 2 consecutive cycles of one drug combination (Cycle X) followed by a cycle of another combination (Cycle Y). On Cycle X, vincristine, and Mesna will be given on day 1 of weeks 1, 4, 10, 13, 19, 22, 28, 31, 27, 40, 49, 55, 58, 64, and 67. On day 2 patients will receive cyclophosphamide and Mesna. On days 3-15 patients will receive G-CSF. On Days 8 and 15, vincristine will be given. Cycle Y will be given on weeks 7, 16, 25, 34, 43, 52, 61 and 70. On Day 1 of Cycle Y, cisplatin will be given. VP-16 will be given on days 3 and 4. On days 5-14 G-CSF will be administered.

Patients experiencing progression or recurrence of disease at any time during or within 12 months of chemotherapy will be encouraged to begin radiation therapy immediately. If disease recurs later than 12 months after completing chemotherapy, patients will be discontinued from the study.

**Progress:** One patient was enrolled in July 94 and continues to be followed.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/146	<b>Status:</b> On-going
<b>Title:</b> POG 9239: Treatment of Children with Newly-Diagnosed Brain Stem Glioma (BSG) Using Cisplatin as a Radiosensitizer with Either Conventional or Hyperfractionated Radiotherapy. A Phase III Study.		
<b>Start Date:</b> 07/01/94	<b>Est. Completion Date:</b>	
<b>Department:</b> POG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Shirley E. Reddoch, MC		
<b>Associate Investigators:</b> COL Bruce A. Cook, MC		MAJ Stephen R. Palmer, MC
<b>Key Words:</b> Cancer:glioma, cisplatin, radiotherapy		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	/ /

**Study Objective:** To compare the time to neurologic and/or radiographic progression and overall survival in children with newly-diagnosed brain stem glioma (BSG) who are treated with 100mg/m<sup>2</sup> of infusional cisplatin combined with conventional vs hyperfractionated radiotherapy; and to determine the toxicities of combining 100mg/m<sup>2</sup> of infusional cisplatin as a radiosensitizer with already-tested radiotherapy fractionation regimens.

**Technical Approach:** This study will evaluate the effectiveness of combining a drug called cisplatin, to be given continuously by vein (IV) over a period of 5 days in combination with either standard radiation treatments given once a day or hyperfractionated (twice daily) radiation treatments. In the first, third, and fifth weeks of radiation therapy, patients will be given a continuous infusion of cisplatin IV over 5 days. The cisplatin infusion will begin at the same time that the radiotherapy begins on that week.

**Progress:** No patients have been enrolled in this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/172		<b>Status:</b> On-going
<b>Title:</b> POG 9262: A Phase II Study of Taxol in Children with Recurrent/Refractory Soft-Tissue Sarcoma, Rhabdomyosarcoma, Osteosarcoma, Ewing's Sarcoma, Neuroblastoma, Germ Cell Tumors, Wilms' Tumor ...				
<b>Start Date:</b> 09/02/94		<b>Est. Completion Date:</b> Jun 97		
<b>Department:</b> POG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Shirley E. Reddoch, MC				
<b>Associate Investigators:</b> COL Bruce A. Cook, MC		MAJ Stephen R. Palmer, MC		
<b>Key Words:</b> Cancer:solid tumors, taxol				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//

**Study Objective:** (1) To determine the response rate of recurrent bone and soft tissue sarcomas, neuroblastoma, germ cell tumors, hepatoblastoma, and hepatocellular carcinoma to taxol in a phase II trial. (2) To further define the spectrum of taxol's toxicity in children and adolescents.

**Technical Approach:** Patients will be premedicated with dexamethasone and diphenhydramine. Taxol will be given intravenously continuously over a 24 hour period. This course will be repeated every 21 days. This treatment may continue for one year, depending on the progression of the disease.

**Progress:** One patient was enrolled at MAMC (FY94). This patient requested removal from the study to seek surgical procedure and eventually died from the underlying disease. Wilm's Tumor is the only treatment arm remaining open to patient accrual.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/072	<b>Status:</b> On-going
<b>Title:</b> POG 9317: Chemotherapy for Children with Advanced Stage (III/IV) Diffuse Undifferentiated Burkitt's Lymphoma and B Cell ALL		
<b>Start Date:</b> 03/04/94	<b>Est. Completion Date:</b> May 99	
<b>Department:</b> POG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Shirley E. Reddoch, MC		
<b>Associate Investigators:</b> COL Bruce A. Cook, MC		MAJ Stephen R. Palmer, MC
<b>Key Words:</b> Cancer:Burkett's lymphoma, ARA-C, cytoxan, Vincristine, Adriamycin, Methotrexate, VP-16, Ifosfamide		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objective:** 1) To evaluate the efficacy of adding VP-16/Ifosfamide intensification to the treatment of patients with advanced-stage B-cell malignancies: Stage III & IV DU NHL and B-cell acute lymphoblastic leukemia (B-ALL). 2) To compare the toxicity and efficacy of high-dose Ara-C given by intermittent bolus (q 12 hour x 4) vs bolus/continuous infusion over 48 hours.

**Technical Approach:** In this groupwide protocol, we propose to add, in a randomized study, two agents active in the treatment of aggressive NHL: Ifosfamide 2.8 g/m<sup>2</sup> with VP-16 100 mg/m<sup>2</sup> qd x 5. All patients in this study will be randomized at diagnosis to receive, throughout therapy, high-dose Ara-C by continuous infusion (CI) or by bolus (actually a 3 hour infusion). The CI Ara-C dose is base on the POG pilot study #9190 with a starting dose of 3.8 g/m<sup>2</sup>/48 hours (80 mg/m<sup>2</sup>/hr) following 9.5 g/m<sup>2</sup> bolus. The bolus Ara-C dose is taken from POG #8617: 3 g/m<sup>2</sup> q 12 hr X 4 doses. All patients will receive therapy based on POG #8617/8616, with a reduction in duration. After a common induction with fractionated cyclophosphamide, vincristine, Adriamycin, methotrexate by 24-hour infusion, and Ara-C, patients with Stage III disease will receive these drugs without Adriamycin and patients with Stage IV/B-ALLL will receive these 5 drugs including Adriamycin during consolidation. Patients will also be randomized to receive or not to receive VP-16/ifosfamide intensification, except for patients with CNS involvement who will be assigned to receive VP/16 ifosfamide. The study question is being posed in a randomized 2 X 2 factorial design.

**Progress:** No patients have been enrolled in this study at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/168		<b>Status:</b> On-going	
<b>Title:</b> POG 9323: Interferon-Alpha 2b Plus Hydroxyurea and Ara-C for Chronic Phase ACML in Children, A POG Pilot Study					
<b>Start Date:</b> 07/21/95			<b>Est. Completion Date:</b> Jul 99		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Shirley E. Reddoch, MC					
<b>Associate Investigators:</b> COL Bruce A. Cook, MC			MAJ Stephen R. Palmer, MC		
<b>Key Words:</b> Cancer:Leukemia, ACML, inteferon, hydroxyurea, Ara-C					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		//	

**Study Objective :** 1) To assess the toxicity of the combination of Hydroxyurea (HU) and Ara-C combined sequentially with interferon-alpha 2b (IFN) in children with adult type chronic myelogenous leukemia (ACML). 2) To determine the frequency and duration of hematologic and cytogenetic response, and the length of time needed to achieve response during two years of such treatment.

**Technical Approach :** Therapy will be divided into 2 induction phases and a consolidation phase. Induction 1: Therapy will begin with two, or possibly three, weekly courses of hydroxyurea and Ara-C. Each course will consist of treatment given on three consecutive days as follows: after consuming clear fluids only for breakfast, hydroxyurea will be taken by mouth. Two hours later, Ara-C will be administered intravenously over 15 minutes. This will be repeated on the second and third day of each course. Subjects will receive at least two courses, beginning days 1 and 8. If blood counts are still above certain values on day 15, a third course will be given. Induction 2: Once blood counts have adequately recovered from the above chemotherapy, IFN treatment will begin. Subjects will receive IFN given as a subcutaneous injection daily for 14 days. Consolidation: IFN will then be continued at this dosage every Monday, Wednesday and Friday. IFN therapy will be interrupted for at least one week, approximately every 6 weeks, for a threeday course of hydroxyurea/Ara-C. This six-week cycle (IFN three times weekly for five weeks followed by a course of hydroxyurea/Ara-C), will be repeated for a total treatment time of approximately two years, assuming a good response to treatment. Most therapy will be administered at home (IFN) or in the outpatient clinic (hydroxyurea/Ara-C), with the exception being the first course of hydroxyurea/Ara-C and the first few days of IFN therapy, for which hospitalization is recommended. Every effort will be made to continue treatment for at least 90 days. All patients who have signs of progressive (worsening) disease within the first 90 days will be evaluated for possible discontinuation of this therapy. All other patients will continue on treatment for a total of 24 months. For those patients continuing on therapy past 90 days, the treatment will be discontinued (prior to 24 months) if there are signs of progressive disease at any time; if there is no evidence of any improvement by six months or if side effects develop which cannot be tolerated even with reduction in the drug dosages. Therapy may also be stopped at any time if a suitable marrow donor has been found and the physician decides that bone marrow transplantation would be in the patient's best interest. If the patient is still on therapy and responding well after 24 months, then the physician may offer to continue therapy with IFN alone. This will be offered as further therapy, but it will not be part of this study. It is not known how many years interferon may be safely given. The dosage

schedule described above is to be considered a guideline. It is very possible that modification will need to be made depending on the side effects encountered.

Routine blood tests will be done during the first four to six weeks of therapy (the "induction" phase), and then every one to two weeks while on therapy. A bone marrow aspirate and biopsy will be done prior to start of induction therapy, then twice more at about three month intervals, and then every six months thereafter unless removed from the study because of no response, progressive disease (increased severity), or bone marrow transplantation. A Chromosomal analysis will be completed on each bone marrow aspirate to find out if the Philadelphia chromosome is present. Each bone marrow aspirate will be followed by an ultrasound study of the spleen in order to determine the size of the spleen.

Progress : One patient was enrolled in this study at MAMC in FY95 and continues to be followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/134		<b>Status:</b> On-going	
<b>Title:</b> POG 9340/41/42: Treatment of Patients Greater than or = 365 Days At Diagnosis With Stage 4 and N-MYC Amplified Stage 2B/3 Neuroblastoma; A Pediatric Oncology Group Phase II Study					
<b>Start Date:</b> 07/02/93			<b>Est. Completion Date:</b> Aug 95		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Shirley E. Reddoch, MC					
<b>Associate Investigators:</b> MAJ Stephen R. Palmer, MC			COL Stephen R. Stephenson, MC COL Bruce A. Cook, MC		
<b>Key Words:</b>					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 02/04/94

**Study Objective:** 1) 9340 Stage 4 (only) - 1.1) To evaluate the response rate to and toxicity of Phase II single-agent chemotherapy (either continuous infusion Adriamycin, or Taxol) given prior to Phase III therapy to two successive subsets of untreated patients  $\geq 365$  days of age with INSS Stage 4 neuroblastoma (NB). 2) 9341-2 Stage 5 and N-myc amplified Stage 2B or 3 (Stage C) - 2.1) To measure response rates and toxicity, event-free survival (EFS), survival, and patterns of failure, of patients treated with 6 courses of induction chemotherapy: high dose platinum/VP-16 (HDP/VP), cyclophosphamide/Adriamycin/ vincristine (CAV), ifosfamide/VP (IFOS/VP), CBDCA/VP, HDP/VP, and CAV plus G-CSF, followed by local radiotherapy and autologous bone marrow transplantation (ABMT) (POG #9342). 2.2) To measure response rates, toxicity, EFS, survival, and patterns of failure of patients whose families decline ABMT, and therefore receive an additional 5 courses of therapy (IFOS/VP, CAV, HDP/VP, CAV, CBDCA/VP) plus G-CSF followed by local radiotherapy to the tumor bed. 2.3) To further evaluate the toxicity of autologous bone marrow transplantation (ABMT) using cyclophosphamide/VP/CBDCA ablation plus local radiotherapy.(POG #9342) 2.4) To measure EFS, survival, and patterns of failure of patients who achieve a complete response or partial response or mixed response at the end of induction chemotherapy prior to ABMT. 2.5) To further evaluate the biologic parameters of neuroblastoma as required for POG 9047, and to measure MDR-1 protein (P-glycoprotein) levels, which will be obtained at diagnosis and in marrow purgates and/or available tumor tissue during therapy, with correlation to clinical presentation at diagnosis, clinical course, response to therapy, and survival. To study the activity of four cycles of Adriamycin, bleomycin, vincristine and etoposide (ABVE) followed by 2550 cGy irradiation in clinically or pathologically staged I, II and IIIA, Hodgkin's Disease.

**Technical Approach:** Patients participating in this study will initially receive two courses of either Adriamycin (IV continuously over 3 days) or taxol (IV continuously over 24 hours). Following initial treatment, intensive therapy with High-dose combinations of 7 drugs will begin. HDP/VP (High-dose cisplatin and VP-16), CAV (Cyclophosphamide, Adriamycin and Vincristine), IFOS/VP (Ifosfamide and VP-16), CBDCA/VP (Carboplatin and VP-16) are the combinations that will be used.

If, after the High-dose therapy, immunofluorescent testing shows  $< 5\%$  tumor cells the patient will be eligible for autologous bone marrow harvest in preparation for autologous bone marrow transplantation (ABMT). After the marrow is harvested Radiation therapy will be administered to the primary tumor bed. Those refusing

ABMT will also receive local radiation therapy and additional courses of the High-dose drug combinations. Also, patients who do not meet eligibility criteria for ABMT will be given additional courses of CAV, HDP/VP, CAV and CBDCA/VP. Patients going on to ABMT will receive ablation therapy beginning 7 to 10 days following radiation therapy. A prescribed course of VP-16, CBDCA, and Cyclophosphamide will be given, careful hydration insured and, when completed, ABMT will be performed. GM-CSF will be given to all patients to enhance rapid bone marrow recovery. Response to ABMT will be evaluated and follow up continued.

Progress: No patients have been enrolled in this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/092		<b>Status:</b> On-going	
<b>Title:</b> POG 9351/CCG 7921: Trial of Doxorubicin, Cisplatin, and Methotrexate With and Without Ifosfamide, With and Without Muramyl Tripeptide Phosphatidyl Ethanolamine (MTP-PE) for .....Osteogenic Sarcoma					
<b>Start Date:</b> 04/01/94			<b>Est. Completion Date:</b> Jun 99		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Shirley E. Reddoch, MC					
<b>Associate Investigators:</b> COL Bruce A. Cook, MC			MAJ Stephen R. Palmer, MC		
<b>Key Words:</b> Cancer:pediatric, cancer:sarcoma, doxorubicin, cisplatin, methotrexate, Ifosfamide, MTP-PE					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		/ /	

**Study Objective:** 1) To improve the survival of patients with osteogenic sarcoma.;2) To compare the results of a prospective, randomized trial of two chemotherapeutic regimens in the treatment of osteogenic sarcoma.;3) To compare the results of a combined chemotherapeutic regimen (high-dose methotrexate, cisplatin, and doxorubicin) given pre-operatively and post-operatively to a similar regimen using the same drugs and adding ifosfamide.;4) To test whether the early introduction of ifosfamide results in a higher rate of good histologic response at the time of definitive surgery.;5) To determine whether histologic response assessed after longer pre-operative chemotherapy with more drugs predicts disease-free survival with the same power as observed in CCG-782 which used a shorter period of pre-operative chemotherapy and fewer drugs.;6) To determine whether liposomal muramyl tripeptide-phosphatidyl ethanolamine (MTP-PE, CGP 19835a), a stimulator of macrophage function, can improve disease-free survival for patients with osteogenic sarcoma.;7) To determine whether multiple drug resistance gene-encoded P-glycoprotein expression is useful for determine prognosis or assigning therapy.

**Technical Approach:** This study is a phase III, prospective, randomized trial of two chemotherapy regimens for the treatment of newly diagnosed, previously untreated osteogenic sarcoma. One regimen calls for the administration of high-dose methotrexate, doxorubicin, and cisplatin. The other regimen calls for the administration of these agents plus ifoxfamide. Chemotherapy is administered for 10 weeks prior to surgical resection of the primary tumor and any metastatic disease (CCG patients). Patients also are randomly assigned either to receive muramyl tripeptide (MTP-PE) with maintenance chemotherapy or to receive maintenance chemotherapy alone.

**Progress:** No patients have been enrolled in this study at MAMC.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/086		<b>Status:</b> On-going	
<b>Title:</b> POG 9354: A Randomized Phase III Evaluation of Intensified Vincristine, Doxorubicin, Cyclophosphamide, Ifosfamide, and Etoposide in the Treatment of Newly-Diagnosed Ewing's Sarcoma or Primitive ...					
<b>Start Date:</b> 03/17/95			<b>Est. Completion Date:</b> Jun 99		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Shirley E. Reddoch, MC					
<b>Associate Investigators:</b> COL Bruce A. Cook, MC			MAJ Stephen R. Palmer, MC		
<b>Key Words:</b> Cancer:Ewing's sarcoma, Cancer:neuroectodermal, Cancer:bone, Cancer:soft tissue; vincristine, doxorubicin, cyclophosphamide, ifosfamide, etoposide					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		/ /	

**Study Objective:** 1) To compare the event-free survival (EFS) and survival of newly diagnosed patients with Ewing's sarcoma and primitive neuroectodermal tumor (PNET) of bone or soft tissue receiving a 48 week standard regimen of vincristine, cyclophosphamide and doxorubicin alternating with ifosfamide and etoposide with G-CSF to those receiving a 30 week dose intensified regimen of the same chemotherapeutic agents. 2) To assess the diagnostic value and prognostic significance of histologic subtype as defined by routine histology, immunochemistry, electron microscopy, and MIC-2 gene expression. 3) To estimate the frequency of occurrence of serious toxicities and adverse orthopedic outcomes associated with the disease and therapy employed, and to compare them between the regimens. 4) To estimate the occurrence of second malignant tumors in these patients. 5) To determine if event free survival and survival differs between patients with PNET and Ewing's sarcoma, and between PNE and Ewing's sarcoma of bone compared to PNET and Ewing's sarcoma of soft tissue.

**Approach:** Subjects will be assigned to one of the two regimens. Regimen A will use drugs according to the standard treatment for Ewing's Sarcoma. Regimen B will utilize the same drugs, in higher doses, over a shorter time period. It is not clear at the present time which of the treatment regimens is better. Whether randomized to Regimen A or Regimen B, the drugs listed below will be given as follows: Vincristine will be given IV push (into vein, quickly). Cyclophosphamide will be given by IV infusion over 30 minutes, (Regimen A); or 6 hours (Regimen B). MESNA will be given to prevent bleeding from the bladder which can be caused by ifosfamide or cyclophosphamide. It will be given intravenous infusion simultaneously with the cyclophosphamide or ifosfamide and will continue to be infused for 3 hours following the end of the cyclophosphamide or ifosfamide dose. Three additional doses of MESNA will be administered by IV over 15 minutes at 3, 6 and 9 hours following the end of the cyclophosphamide dose. Doxorubicin will be given by continuous infusion over 2 days. G-CSF will be given subcutaneous (SC, into the skin) or IV over 2 hours. Etoposide (VP-16) will be given IV over 1 hour. Ifosfamide will be given IV over 1-3 hours.

**Progress :** No patients have been enrolled in this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/057		<b>Status:</b> On-going	
<b>Title:</b> POG 9360: GM-CSF Randomization Plus High-Dose "ICE" in the Treatment of Recurrent/Resistant Malignant Solid Tumors of Childhood, A pediatric Oncology Group, Phase II Study					
<b>Start Date:</b> 12/16/94			<b>Est. Completion Date:</b> Jan 97		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Shirley E. Reddoch, MC					
<b>Associate Investigators:</b> COL Bruce A. Cook, MC			MAJ Stephen R. Palmer, MC		
<b>Key Words:</b> leukemia:pediatric, solid tumors, carboplatin, GM-CSF, ifosfamide, VP-16					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		//

**Study Objective:** 1) To determine the antitumor activity and toxicity of the maximum-tolerated dose of ifosfamide and carboplatin plus etoposide (high-dose ICD) against childhood and adolescent malignant solid tumors resistant to conventional chemotherapy. 2) To define the most effective but least toxic dose of GM-CSF to be used to ameliorate the myelosuppression that accompanies ICE therapy.

**Approach:** This study involves the administration of three drugs; ifosfamide, carboplatin, and etoposide (VP-16) ("ICE" therapy) which have been shown to be active against these tumors, alone or in combination with other drugs. In addition, you (your child) will be given an investigational protein drug, rhu granulocyte-macrophage colony stimulation factor (GM-CSF), in order to decrease side effects of this treatment. You (your child) will be randomized (assigned by chance; such as the flipping of a coin) to one of two doses of GMCSF.

VP-16 will be given intravenously (into the vein) over 60 minutes, followed by ifosfamide (intravenously) over 3 hours every day for three days. Another drug named MESNA will also be given at specified intervals prior to and after ifosfamide. The purpose of MESNA is to help prevent bleeding from the bladder that can occur with ifosfamide. Carboplatin will be given immediately following ifosfamide, intravenously, over 60 minutes, on day 3 only. GM-CSF will be given subcutaneously (just under the skin) on days 4 to 19 or until the blood counts recover. This course may be repeated one or more times depending upon the response and at the discretion of your (child's) physician. You (your child) will no longer receive treatment with these drugs if your (child's) disease worsens or if there has been no response to treatment, or if unacceptable toxicity occurs. Patients on this study will be followed with medical check-ups for approximately two years in order to monitor response to treatment and long-term survival.

**Progress :** No patients have been enrolled in this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/087		<b>Status:</b> On-going	
<b>Title:</b> POG 9362: A Phase II Study of Alpha Interferon in HIV-Related Malignancies					
<b>Start Date:</b> 03/17/95			<b>Est. Completion Date:</b> Jun 99		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Shirley E. Reddoch, MC					
<b>Associate Investigators:</b> COL Bruce A. Cook, MC			MAJ Stephen R. Palmer, MC		
<b>Key Words:</b> Cancer:all types, HIV, Interferon					
<b>Accumulative</b> <b>MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative</b> <b>OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> / /

**Study Objective:** 1) To Estimate the complete response rate for HIVrelated malignancies treated with interferon (aIFN). 2) The secondary objectives are to estimate the oneyear disease free survival and to evaluate the toxicity of aIFN alone or in combination with anti-retroviral therapy.

**Approach:** This study will require all patients to be enrolled in POG 9182 and compliance with all specimen submission requirements of that protocol. The study will minimize additional tissue, CSF or blood sampling except as required for monitoring for toxicity and tumor response. This study will take advantage of the demonstrated antitumor and antiviral activity of aIFN alone or in combination with other antiretroviral agents to treat HIV positive children with refractory or newly diagnosed malignancies. As the duration of response is one of the goals of this study, responders will continue on therapy indefinitely. Patients on this study will be treated using a interferon by subcutaneous injection every day for 14 days; then if your child's/adolescent's evaluation allows further treatment he/she will receive a interferon three times a week. This treatment will need to be monitored by a treating physician and blood tests will be performed in order to insure that the treatment is well tolerated and that the dose is appropriate. For that purpose 10cc of blood will be taken once a week. The physician and/or staff will be checking closely to see if any of these side effects are occurring. Routine physical exams, laboratory tests and tests such as biopsy or bone marrow aspiration may be necessary to monitor the effect of the treatment. Side effects usually disappear after the treatment is stopped. In the meantime, the doctor may prescribe medication to keep these side effects under control.

**Progress :** No patients have been enrolled in this study at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/088		<b>Status:</b> On-going	
<b>Title:</b> POG 9382: Molecular Studies of t(11;22) Translocation in Ewings' Sarcoma and Peripheral PNET of the Bone					
<b>Start Date:</b> 03/17/95			<b>Est. Completion Date:</b> Jun 99		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Shirley E. Reddoch, MC					
<b>Associate Investigators:</b> COL Bruce A. Cook, MC			MAJ Stephen R. Palmer, MC		
<b>Key Words:</b> Cancer:Ewing's sarcoma, Cancer:neuroectodermal, Cancer:bone					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		/ /	

**Study Objective:** 1) To determine if the presence of minimal metastatic disease as measured by PCR imparts a poor prognosis in patients with localized disease at diagnosis. 2) To determine the prevalence of minimal residual and metastatic disease in the bone marrow and peripheral blood of patients with Ewing's Sarcoma or PPNET as measured by PCR amplification of the t(11;22) chromosomal translocation. 3) To correlate the presence of minimal residual or metastatic disease at diagnosis with other clinical parameters. 4) To determine the types and frequency of chromosomal breakpoints and fusion transcripts and to identify whether certain chromosomal breakpoints correlate with clinical outcome. 5) To determine at what rate patients with clinically documented metastatic disease (at diagnosis or relapse) have evidence of circulating cells with the t(11;22) translocation in peripheral blood, bone marrow, or other body fluids (e.g. CSF, pleural fluid, etc.).

**Approach:** For those subjects who are consented, will have their tumor, blood, and bone marrow looked at for residual disease. An additional blood sample will be obtained just prior to the 2nd course of chemotherapy, and at the completion of the study. Molecular studies will then be performed on these items. Statistical inference will be applied to the primary objective (#1), with descriptive measures being utilized to address the remaining objectives, which are viewed as hypothesis generating. Because of the difficulty in obtaining prior information regarding the PCR measurements, no a prior power calculations can be done. Based on POG 8850, accrual of 45 patients/year could potentially be achieved, for a total of 180 In 4 years. To test whether the presence of minimal metastatic disease as measured by PCR defines a poor risk group, we will conduct three one-sided log-rank tests on event-free survival, using a Bonferroni correction (i.e., each test will use  $\alpha=0.05/3=0.0167$ ). The tests will be done at diagnosis, end of cycle 2, and end of therapy, with the two EFS curves at each time point being defined according to whether the PCR is positive or negative.

**Progress :** No patients have been enrolled in this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/148		<b>Status:</b> Completed
<b>Title:</b> POG 9398: T-4 "D": Efficacy of rhG-CSF in an Intensive Treatment for T-Cell Leukemia and Advanced-Stage Lymphoblastic Lymphoma of Childhood				
<b>Start Date:</b> 07/01/94		<b>Est. Completion Date:</b> May 99		
<b>Department:</b> POG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL Bruce A. Cook, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> Cancer:lymphoma, Cancer:childhood, rhG-CSF, Cancer:leukemia				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//

**Study Objective:** (1) To determine if the addition of high-dose Ara-C and IV methotrexate and 6-mercaptopurine will improve the effectiveness of this combination of anticancer medicine against T-cell acute lymphoblastic leukemia and advanced-stage lymphoblastic lymphoma without being too toxic; (2) whether rhG-CSF can reduce the period of neutropenia, and infectious episodes in a cohort of patients receiving multiagent chemotherapy for T-cell leukemia or lymphoblastic lymphoma; (3) whether after different drug combinations, G-CSF reduces delays in chemotherapy.

**Technical Approach:** Patients will receive vincristine, prednisone, cyclophosphamide and Adriamycin; then cytosine arabinoside with or without cyclophosphamide. All patients will receive a three-drug combination of methotrexate, hydrocortisone, and Ara-C intrathecally to prevent central nervous system disease.

After a disease-free state has been attained, patients will receive a more intense 9-week sequence of drug combinations. This 9-week sequence will be repeated 10 times to complete a total of approximately two years of therapy. Additionally, patients will receive L-asparaginase every week for 20 doses during the 9 week repetitive therapy. Patients will be randomized to receive or not to receive the growth factor G-CSF.

**Progress:** This study closed to patient accrual 15 Dec 94. No patients were enrolled in this study at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/058		<b>Status:</b> On-going	
<b>Title:</b> POG 9400: ALinC 16 Classification (C) Protocol					
<b>Start Date:</b> 12/16/94			<b>Est. Completion Date:</b> Dec 99		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Shirley E. Reddoch, MC					
<b>Associate Investigators:</b> COL Bruce A. Cook, MC			MAJ Stephen R. Palmer, MC		
<b>Key Words:</b> leukemia:pediatric, laboratory classification					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		/ /	

**Study Objective:** 1) To continue to characterize the biologic findings of the acute lymphoblastic and undifferentiated leukemias (immunologic markers, ploidy (DNA index), karyotyping, morphology) and their relationship, as prognostic factors for attaining and maintaining remission.

2) To apply to therapy selection, the determination that ploidy and certain structural chromosomal abnormalities predict poor prognosis.

3) To evaluate the usefulness of PCR technique in detecting minimal residual disease in patients with disease demonstrating t ( 9; 2 2 ) or t ( 1; 19 ) chromosomal abnormalities. (optional)

4) To apply to therapy selection molecular testing for 11q23 translocation in infants < 12 months of age with acute lymphocytic leukemia.

5) To determine the roll of p53 and pl6 tumor suppressor genes in T-ALL. (optional)

6) Individual patient outcome will be compared with the leukemia cell proliferation response to ask if proliferation in response to a myeloid growth factor is associated with an increased risk of developing AML. (optional)

7) To determine risk group assessment using Fluorescent In-Situ Hybridization (FISH) screening for Trisomies 4 and 10 in Non-T, Non B ALL.

8) To determine if drug sensitivity profiles of blast cells for three commonly used chemotherapeutic agents - Adriamycin, Methotrexate, and Cytarabine correlate with a) initial response b) subsequent development of relapse.

**Approach:** A bone marrow aspirate (a needle stick in hip bone to draw marrow into syringe) will be done to prove or disprove diagnosis of leukemia. If leukemia is present, it is important to identity the exact type and subtype of leukemia, in order to plan treatment. This typing requires that several laboratory tests be run on the leukemia cells in the bone marrow. As we perform the bone marrow aspiration we will be removing enough bone marrow (about 2-1/2 teaspoons) to run the laboratory tests. We may also need to draw some blood (about 2-1/2 teaspoons) from a vein to send for studies. Some of these tests will be done here and some will be sent to reference laboratories in other Pediatric Oncology Group institutions for different kinds of special tests to identify the characteristics of the leukemia cells.

**Progress :** Two patients enrolled in this study at MAMC in FY95 and continue to be followed at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/059		<b>Status:</b> On-going	
<b>Title:</b> POG 9405: ALinC 16: Protocol for Patients With Newly Diagnosed Standard Risk Acute Lymphoblastic Leukemia (ALL)					
<b>Start Date:</b> 12/16/94			<b>Est. Completion Date:</b> Dec 99		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Shirley E. Reddoch, MC					
<b>Associate Investigators:</b> COL Bruce A. Cook, MC			MAJ Stephen R. Palmer, MC		
<b>Key Words:</b> leukemia:peds, leukemia:lymphoblastic, Calcium leucovorin, cytosine arabinoside, E. coli L-asparaginase, Erwinia L-asparaginase, hydrocortisone, 6-mercaptopurine, methotrexate, prednisone, vincristine					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		//

**Study Objective:** 1) To determine in a randomized trial, the efficacy of a higher (2.5 gms/mt) versus standard (1 gm/m2) dose methotrexate (MTX) infusion during consolidation. The major endpoint will be eventfree survival among those achieving a complete remission. Secondary comparisons will include sitespecific events and adverse drug reactions.

2) To determine in a randomized comparison, the efficacy of delivering oral 6-MP on a once versus twice daily schedule during continuation.

3) To study laboratory correlates from POG 9400 and clinical correlates with outcome in pooling studies 9201, 9405 and 9406.

4) To assess the prognostic significance of the percent of marrow blasts after two weeks of induction therapy.

**Approach:** In this research study, the subject will receive intensive combination chemotherapy for 4 weeks to eliminate visible disease (remission induction). This induction chemotherapy involves standard combinations of such agents as Prednisone, given orally (by mouth) for 28 days; vincristine, given by a quick intravenous infusion (IV push) on days 1, 8, 15, and 22; L-asparaginase, injected into a muscle (IM) on days 2, 5, 8, 12, 15, and 19. The drugs methotrexate, Ictosine arabinoside (Ara-C), and hYdrocortisone will be administered intrathecally (injected into the spinal fluid) at various intervals throughout both the induction and intensive periods to prevent the leukemia from coming back in the central nervous system.

After Induction the subject will be randomized (assigned by chance, such as flipping a coin), to a specific regimen to include either standard or high dose IV Methotrexate and receiving oral 6MP once or twice daily. During the period of consolidation (weeks 5-28), the subject will receive the drugs methotrexate and 6-mercaDtpurine (6-MP). The Methotrexate will be given at a standard or higher dose. In the first week, methotrexate will be injected into a vein followed by a 24-hour infusion. The vitamin Leucovorin will be given orally or as an infusion to help protect the patient from the toxicity of methotrexate. Immediately after the methotresate, 6-MP will be given by IV infusion over 20 minutes followed by an infusion over 6 hours. On the second week of therapy, the subject will receive methotrexate injected into a muscle (IM) on day 1 and 6-MP daily by mouth for 7 days. This 2 week treatment will be repeated for a total of 12 cycles. During the period of continuation (weeks 20-130), 6-MP will be given orally each day, and methotrexate injected into a muscle (IM) once each week. Patients randomized onto regimens B & D will receive 6MP orally twice

daily.

The subject will be taken off study in case of relapse in the bone marrow, or any other site, or if the subject fails to achieve a complete remission during the induction phase of the study.

At the time of bone marrow aspiration, blood sampling, or spinal tap, cells obtained may be used for research studies. These studies will help the doctor to better understand this form of cancer and how treatment can be improved in the future. Chemotherapy given intrathecally into the spinal fluid may cause pain at infusion site, pain in the back, legs or head, fever, headache, vomiting; rarely stiff neck, convulsions, paralysis. Bone marrow aspiration may cause bruising and soreness over the bone from which the marrow sample is taken.

Progress : One patient was enrolled in this study at MAMC in FY95 and continues to be followed.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/060	<b>Status:</b> On-going
<b>Title:</b> POG 9406: ALinC #16 - Protocol for Patients With Newly Diagnosed High Risk Acute Lymphoblastic Leukemia (ALL)		
<b>Start Date:</b> 12/16/94	<b>Est. Completion Date:</b> Dec 99	
<b>Department:</b> POG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Shirley E. Reddoch, MC		
<b>Associate Investigators:</b> COL Bruce A. Cook, MC		MAJ Stephen R. Palmer, MC
<b>Key Words:</b> leukemia:pediatric, calcium leucovorin, ARA-C, E. coli asparaginase, Erwinia asparaginase, PEG asparaginase, hydrocortisone, Daunomycin, 6-mercaptopurine, methotrexate, prednisone, vincristine, VM-26		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	/ /

**Study Objective:** 1) To determine the efficacy of a 2.5 gm/m<sup>2</sup> dose versus 1 gm/m<sup>2</sup> does intravenous methotrexate infusions during intensified continuation therapy. The major endpoint will be event-free survival among those achieving a complete remission. Secondary comparison will include site-specific events and adverse drug reactions. 2) To determine whether intensified continuation therapy delivering pulses of Ara-C (3 gm/m<sup>2</sup> x 4 doses) with asparaginase rescue is superior to standard intensified continuation with pulses of VM-26/Ara-C. The major endpoint will be event-free survival among those achieving a complete remission. Secondary comparison will include site-specific events (including secondary AML) and adverse drug reactions. 3) To study laboratory correlates from POG 9400 and clinical correlates with outcome in pooling studies 9201, 9405, and 9406. 4) To assess the prognostic significance of the percent of marrow blasts after two weeks of induction therapy.

**Approach:** In this research study, a child will receive intensive combination chemotherapy for 4 weeks to eliminate visible disease (remission induction). This induction chemotherapy involves standard combinations of such agents as prednisone, given orally for 28 days; vincristine, given by a quick intravenous infusion on days 1, 8, 15, and 22; L-asparaginase, injected IM on days 2, 5, 8, 12, 15, and 19. The drugs methotrexate, cytosine, arabinoside (Ara-c), and hydrocortisone will be administered intrathecally at various intervals throughout the induction and intensive periods to prevent the leukemia from coming back in the central nervous system. Daunomycin will be given on days 8, 15, and 22 intravenously. After the previous treatment, subjects will be randomized to a specific regimen to include either standard or high dose Methotrexate or low or high dose Ara-C. During the period known as consolidation, the subject will receive the drugs methotrexate and 6-mercaptopurine (6-MP) during weeks 5-6, 10-11, 15-16, 25-26, and 30-31. In the first week of each of these periods, methotrexate (either the standard or the intensified higher dose) will be injected into a vein followed by a 24-hour infusion. The vitamin Leucovorin will be given orally or as an infusion to help protect the patient from the toxicity of methotrexate. Immediately after the methotrexate, 6-MP will be given by IV infusion over 20 minutes followed by an infusion over 6 hours. On the second week of therapy, the subject will receive methotrexate injected into a muscle (IM) on day 1 and 6-MP daily by mouth for 7 days.

At weeks 7, 17, and 27 the subject will receive Ara-C as a continuous infusion for 72 hours (higher dose) or injected under the skin (lower dose). VM-26 will be given as a

45-minute IV infusion before the start of Ara-C and on day 2 with standard dose Ara-C. If the subject receives intensified Ara-C, the subject will also receive the drugs PEG and G-CSF. PEG is a drug that may lessen the toxic effects of Ara-C, and G-CSF is used to increase the blood count to decrease the risk of infection.

At weeks 12, 22, and 32, Ara-C will be infused over 72 hours as described above. Daunomycin (DNR) will be given as a 30-minute infusion before the start and at the end of the Ara-C. In addition to DNR/Ara-C, vincristine is given IV on days 1 and 8, prednisone by mouth on days 1 and 7, and PEG-L-asparaginase IM on day 1.

During the period known as continuation, weeks 35-130, standard dose 6-MP will be given orally each day, and methotrexate injected into a muscle (IM) once a week. The total time of planned therapy is 130 weeks (2 1/2 years).

The subject will be taken off study in case of relapse in the bone marrow, or any other site, or if the subject fails to achieve a complete remission during the induction phase of the study. Radiation therapy will be suggested if the subject has CNS leukemia at diagnosis.

At the time of bone marrow aspiration, blood sampling, or spinal tap, cells obtained may be used for research studies.

Progress : No patients were enrolled in this study at MAMC in FY95, however one patient registered on this study was accepted in transfer from SUNY and continues to be followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/089		<b>Status:</b> On-going	
<b>Title:</b> POG 9421: Phase III Evaluation of Standard vs. High Dose ARA-C Induction Followed by the Randomized Use of Cyclosporine A As An MDR Reversal Agent, Compared to Allogeneic BMT, in Childhood AML					
<b>Start Date:</b> 03/17/95			<b>Est. Completion Date:</b> Jan 01		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Shirley E. Reddoch, MC					
<b>Associate Investigators:</b> COL Bruce A. Cook, MC			MAJ Stephen R. Palmer, MC		
<b>Key Words:</b> Cancer:AML, ARA-C, Cyclosporine, multidrug resistance					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> / /

**Study Objective:** 1) To determine the effect of high dose vs. standard dose Ara-C induction on CR (clinical remission) and EFS (event free survival) in Childhood AML. 2) To compare EFS in Childhood AML after 3 cycles of consolidation with or without the MDR (multidrug resistance) modulator CSA (cyclosporine A). 3) To compare the EFS between patients genetically randomized between allogeneic BMT and chemotherapy. 4) To evaluate the impact of EFS of various clinical and laboratory factors such as cytogenetics and MDR expression. 5) To confirm the superior response of Down syndrome patients utilizing standard induction and non-CSA containing consolidation, and identify specific biologic and pharmacokinetic characteristics in these patients.

**Approach:** Phase III evaluation of standard vs. high dose Ara-C induction followed by the randomized use of Cyclosporine A as an MDR (multidrug resistant) reversal agent, compared to allogeneic BMT, in childhood AML. Patients will be randomized (assigned by chance, such as flipping a coin) at the time of diagnosis to receive either standard doses or high doses of ARA-C during the initial course of therapy. The chances of receiving any of the therapies is approximately equal. Later in the course of therapy, patients (according to how they were previously randomized) will or will NOT receive the drug Cyclosporine A in combination with the chemotherapy agents, Mitoxantrone and Etoposide. Patients with Down syndrome will not be randomized, but will receive the standard therapy. Earlier studies have shown the three year event-free survival rate for Down syndrome children significantly superior to children without Down syndrome using standard therapy. Also, for this reason Down syndrome patients will not receive Cyclosporine A. If a sibling who is matched for bone marrow transplantation, will receive bone marrow transplantation, which has been shown to be a more effective treatment in controlling AML compared to chemotherapy, providing that consent from the sibling donor can be obtained. If not a sibling donor, studies have shown chemotherapy is superior to matched unrelated donor BMT. However, should the patient choose to pursue an unrelated matched BMT instead of continuing with consolidation chemotherapy, the subject may discontinue the study. At the time of bone marrow aspiration, blood sampling, or spinal tap, cells obtained may also be used for research studies.

**Progress :** No patients have been enrolled in this study at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/186		<b>Status:</b> On-going	
<b>Title:</b> POG 9450: Etoposide/Ifosfamide + G-CSF in the Treatment of Newly Diagnosed Metastatic Osteosarcoma or Unresectable Osteosarcoma					
<b>Start Date:</b> 09/15/95			<b>Est. Completion Date:</b> Jan 99		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Shirley E. Reddoch, MC					
<b>Associate Investigators:</b>			MAJ Stephen R. Palmer, MC		
LTC Luke M. Stapleton, MC			MAJ Kenneth A. Bertram, MC		
MAJ Robert B. Ellis, MC			CPT James S. D. Hu, MC		
LTC Robert D. Vallion, MC			MAJ Richard F. Williams, MC		
CPT John R. Caton, MC					
<b>Key Words:</b> Cancer:osteosarcoma, etoposide, ifosfamide, G-CSF					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		/ /	

**Study Objective:** 1) To estimate the response rate to etoposide (VP-16), ifosfamide (IFOS) and G-CSF in patients presenting with newly-diagnosed metastatic or unresectable osteosarcoma prior to treatment with other chemotherapeutic agents. 2) To evaluate the toxicity of VP-16/IFOS in newly diagnosed patients. 3) To estimate the duration of survival for patients presenting with newly-diagnosed metastatic osteosarcoma or unresectable osteosarcoma who are treated with a multi-agent chemotherapy regimen preceded by induction therapy with VP-IFOS and G-CSF. 4) To determine the ability of pathologic primary tumor response from 2 courses of pre-surgical chemotherapy to predict outcome as measured by time to disease progression, disease free survival and survival.

**Technical Approach :** This study involves treatment with the combination of drugs etoposide (VP-16) and ifosfamide (IFOS) at high doses. Granulocytic Colony Stimulating Factor (G-CSF) will be used to help the patient's bone marrow white cells recover faster after each of the first 2 courses of high dose VP-16 and IFOS, and thereafter as necessary. This study will determine the response rate of high dose VP-16/IFOS in the treatment of osteosarcoma and will try to determine whether this high dose combination will improve the overall outcome of this group of high risk patients. Patients will also receive these drugs in standard dosing during continuation therapy in combination with other chemotherapy drugs which are used to treat osteosarcoma. VP-16 will be given intravenously over 60 minutes, followed by intravenous ifosfamiti over 4 hours every day for 5 days. Another drug, MESNA will also be given at specified intervals with and after ifosfamide. The purpose of MESNA is to help prevent bleeding from the bladder which can occur with ifosfamide. G-CSF will be given subcutaneously (injected under the skin) once a day, starting on the day the chemotherapy finishes and continuing until blood counts return to normal. This course will be repeated one more time (approximately 3 weeks later). After 6 weeks, patient will be re-evaluated (x-ray, MRI, CT) to determine the response to this drug combination. If possible, all sites of remaining tumor will then be removed surgically. After surgery, chemotherapy will resume with a combination of drugs (methotrexate. ifosfamide. VP-16 adriamycin and cisplatin) which have been proven to be effective against osteosarcoma. The vitamin Calcium Leucovorin will be given along with the methotrexate. Treatment will then continue for approximately one year.

**Progress :** No patients have been enrolled in this study at MAMC.

**DETAIL SHEETS FOR PROTOCOLS**

**PUGET SOUND ONCOLOGY CONSORTIUM**

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 91/066	<b>Status:</b> Completed
<b>Title:</b> PSOC 1007: Adriamycin and Cefoperazone for Treatment of Carcinoma and Sarcoma Refractory to Adriamycin		
<b>Start Date:</b> 06/14/91	<b>Est. Completion Date:</b>	
<b>Department:</b> PSOC	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Paul C. Sowray, MC		
<b>Associate Investigators:</b>		
MAJ William A. Phillips	LTC Howard Davidson, MC	
MAJ Everardo E. Cobos Jr., MC	LTC Luke M. Stapleton, MC	
MAJ Robert L. Sheffler, MC	MAJ Patrick L. Gomez, MC	
CPT Jennifer L. Cadiz, MC	MAJ Robert B. Ellis, MC	
<b>Key Words:</b> adriamycin,cefoperazone		
<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	//

**Study Objective:** To determine the complete and partial response rates to a combination of adriamycin and cefoperazone in patients who have had progression of non-Hodgkin's lymphoma, small cell lung carcinoma, sarcoma, breast or ovarian carcinoma while on an adriamycin-containing chemotherapeutic regimen or have progressed within six months of receiving such a regimen and to determine the toxicities of the addition of high dose cefoperazone to adriamycin in the treatment of refractory malignant disease.

**Technical Approach:** Adriamycin has been used extensively in the therapy of a number of malignancies. In many instances, the malignant cells become resistant and adriamycin becomes ineffective and is one of the agents implicated in multiple drug resistance (MDR). Because of its clinical value, the mode of action of adriamycin and the possible mechanisms of drug resistance have been the subject of extensive research. Cefoperazone has been purported to act as a modulator of MDR. It is hoped that high-dose cefoperazone will block the MDR capability of the cancer cells which will allow the adriamycin to remain within the cancer cells for a longer period of time, thereby allowing patients to go back into remission. All patients will receive intravenous cefoperazone weekly at a dose of 5 grams in 30 minutes, followed by a continuous IV infusion for three hours at 4 grams per hour. After the 30 minutes loading dose, patients will be given a bolus of adriamycin. Patients will be reevaluated after eight weeks. Patients will continue on treatment until there is evidence of disease progression; there is a decrease in ejection fraction by MUGA scan to <40% or a fall of 20 percentage points; or the patient develops symptoms of congestive heart failure.

**Progress:** One patient entered in FY 91, expired 5 Apr 1995.

**DETAIL SHEETS FOR PROTOCOLS**

**RADIOLOGICAL DIAGNOSTIC ONCOLOGY GROUP**

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/136		<b>Status:</b> On-going	
<b>Title:</b> RDOG(5) 6881: Stereotactic Fine Needle Aspiration Biopsy and Core Needle Biopsy in the Work-up of Lesions Detected by Mammography					
<b>Start Date:</b> 06/16/95			<b>Est. Completion Date:</b> Jun 98		
<b>Department:</b> RDOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL Sankaran S. Babu, MC					
<b>Associate Investigators:</b> MAJ Vincent B. Ho, MC COL Preston L. Carter, MC			Charlene P. Holt, M.D. MAJ William C. Williard, III, MC MAJ Barbara A. Crothers, MC		
<b>Key Words:</b> Cancer:breast, FNA, Core biopsy, mammography					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		/ /	

**Study Objectives:** The overall objective of this research protocol is to conduct a randomized clinical trial to study whether stereotactically-guided and/or ultrasound-guided fine needle aspiration (FNA) and/or core needle biopsy (CNB) can replace open surgical biopsy in the diagnostic evaluation of nonpalpable mammographically-detected breast lesions.

**Technical Approach:** This is a randomized clinical trial to be carried out in mammographic centers nationwide within two consortia. This offers the opportunity to cover the spectrum of experience, equipment and patient populations, all using an agreed protocol to evaluate the use of fine needle and core biopsy used in the work-up of non-palpable breast lesions. The two consortia will enroll a total of 3,600 patients with an expected average MAMC enrollment of two subjects per day for the length of the study. Women having had the appropriate mammographic evaluation and meeting the inclusion criteria will be entered either to stereotactic or ultrasound arms of the study. Those in the stereotactic arm will be randomized to FNA followed by CNB, or CNB alone, both followed by open surgical biopsy or when indicated, 6, 12, and 24 month follow-ups. Those in the ultrasound arm will be randomized to FNA/CNB or CNB. All mammograms will have second readings by experts, and all pathology and cytology will have second readings by reference experts. Data analysis will consist of accuracy determination, agreement analysis, and logistic regression modeling for evaluation of important co-variants on the estimates. In addition, analysis of observer variability, insufficient sample rates, and predictive ability of specific mammographic characteristics will be conducted.

**Progress :** No subjects entered at MAMC.



**DETAIL SHEETS FOR PROTOCOLS**

**SOUTHWEST ONCOLOGY GROUP**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 77/054		<b>Status:</b> On-going	
<b>Title:</b> SWOG 7406: Advanced Hodgkin's Disease: Remission Induction (MOPP #5). Phase III					
<b>Start Date:</b> 02/18/77			<b>Est. Completion Date:</b> Feb 82		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC					
<b>Associate Investigators:</b> COL Friedrich H. Stutz, MC			LTC H. Irving Pierce, MC		
<b>Key Words:</b> Cancer: Hodgkin's, MOPP					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		12/17/93

**Study Objective:** (1) To compare the effectiveness of two MOPP (nitrogen mustard, vincristine, procarbazine, and prednisone) + bleomycin + adriamycin combinations against MOPP + bleomycin for remission induction in patients with advanced Hodgkin's disease without prior chemotherapy; (2) To evaluate systematic restaging of patients in apparent complete remission; (3) To assess the length of unmaintained remission after intensive induction with ten courses of treatment and after documentation of complete remission (CR) status by careful restaging; (4) To evaluate by crossover design the remission induction potential of the other study combinations for patients who relapse during unmaintained remission.

**Technical Approach:** All previously untreated patients with Ann Arbor Stages IIIB or IV A+B Hodgkin's disease who meet the other criteria as outlined in the protocol will be randomized to one of the induction programs as specified in the protocol. Ten courses of treatment at 4-week intervals will constitute remission induction. If induction results in a CR and this is confirmed by restaging, then no further treatment will be given. If at least a partial remission (PR) is indicated another 4 courses will be administered in a second attempt to achieve a CR. Persistence of disease after 14 courses will constitute an induction failure and the patient will be taken off study. Relapsing patients will be crossed over to one of the other induction combinations.

**Progress:** Closed to patient entry 31 Aug 78. Two patients were entered in previous years, one patient is still being followed.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 77/053		<b>Status:</b> On-going	
<b>Title:</b> SWOG 7433: Non-Hodgkin's Lymphomas (Stages I, IE, II, and IIE). A Phase III Study.					
<b>Start Date:</b> 02/18/77			<b>Est. Completion Date:</b> Feb 82		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC					
<b>Associate Investigators:</b> COL Friedrich H. Stutz, MC			LTC H. Irving Pierce, MC		
<b>Key Words:</b> Cancer:Non-Hodgkin's lymphoma, radiotherapy, CHOP					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 11/18/94

**Study Objective:** To compare the remission rate, remission duration and survival in patients with non-Hodgkin's lymphoma, pathologic stages I, IE, II and IIE treated with extended field radiotherapy (supradiaphragmatic mantle or abdominal field) alone or with extended Hydroxyl-daunorubicin (adriamycin), Oncovin (vincristine), and Prednisone.

**Technical Approach:** Patients newly diagnosed (no type of prior therapy) with non-Hodgkin's lymphoma except mycosis fungoides and diffuse lymphocytic well differentiated lymphoma will be thoroughly evaluated for extent of disease and then randomized to either radiation therapy or radiation therapy plus chemotherapy. If the patient does not achieve a complete remission after completion of his treatment course, he will be removed from the study. Those achieving complete remission will be followed for two years or until relapse.

**Progress:** This protocol was closed to patient entry 1 Oct82 and was previously reported as closed. In fact, 2 patients were entered at MAMC, 1 has died and the other is still being followed. The protocol was reactivated in December 1993 in order to allow SWOG to continue to collect data on these patients.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 77/024		<b>Status:</b> On-going
<b>Title:</b> SWOG 7436: Combined Modality Therapy of Breast Cancer				
<b>Start Date:</b> 01/21/77			<b>Est. Completion Date:</b> Jan 82	
<b>Department:</b> SWOG			<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Howard Davidson, MC				
<b>Associate Investigators:</b> LTC H. Irving Pierce, MC			COL Friedrich H. Stutz, MC	
<b>Key Words:</b> Cancer:breast, 5-FU, vincristine, methotrexate, cyclophosphamide, prednisone				
<b>Accumulative MEDCASE Cost:</b> \$0.00		<b>Est. Accumulative OMA Cost:</b> \$0.00		<b>Periodic Review:</b> 11/18/94

**Study Objective:** To compare the effect of two adjuvant chemotherapy programs upon the time to recurrence and upon the percentage of recurrences in post-operative breast carcinoma patients who have a high risk of developing metastases. To compare the effect of these adjuvant chemotherapy programs upon the survival pattern of such patients.

**Technical Approach:** Melphalan and combination (5-Fluorouracil, Methotrexate, Vincristine, Cyclophosphamide, Prednisone) will be used as chemotherapy as outlined in the protocol. The adjuvant chemotherapy will be instituted (regardless of radiation therapy) two weeks after radical mastectomy, unless local or systemic post-operative complications of surgery contraindicate onset of therapy. In such cases, therapy will be instituted when the primary physician involved feels it is not contraindicated by the clinical condition of the patient. The interval between surgery and the institution of adjuvant chemotherapy cannot be greater than six weeks for entry into the study. All therapy will be discontinued after one year.

**Progress:** This protocol was closed to patient entry in November 1979 and was previously reported as closed. In fact, 10 patients were entered at MAMC, 4 have died, and 6 patients are still being followed. The protocol was reactivated in December 1993 so that SWOG could continue to collect data on these patients.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 77/018		<b>Status:</b> On-going
<b>Title:</b> SWOG 7510: Intensive Adjuvant Chemotherapy with or without Oral BCG Immunotherapy for Patients with Locally Advanced Adenocarcinoma of the Large Bowel				
<b>Start Date:</b> 10/15/76		<b>Est. Completion Date:</b> Oct 81		
<b>Department:</b> SWOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC				
<b>Associate Investigators:</b> COL Friedrich H. Stutz, MC		LTC H. Irving Pierce, MC		
<b>Key Words:</b> Cancer:bowel, chemotherapy, BCG immunotherapy				
<b>Accumulative MEDCASE Cost:</b> \$0.00		<b>Est. Accumulative OMA Cost:</b> \$0.00		<b>Periodic Review:</b> 11/18/94

**Study Objective:** To determine the efficacy of adjuvant chemotherapy with the highly effective combination of Methyl CCNU (MeCCNU) and 5-Fluorouracil (5-FU) and to determine whether this is added to by immunotherapy with oral Bacillus Calmette-Suerin (BCG) on the disease-free interval and survival of patients with Duke C large bowel adenocarcinoma.

**Technical Approach:** Patients will be randomly assigned to either of the two following regimens; (1) chemotherapy alone - Methyl CCNU, given orally on day 1, plus intravenous 5-Fluorouracil, given intravenously weekly for three doses would constitute one course. Courses would be every eight weeks; (2) chemotherapy plus immunotherapy - Chemotherapy as described above plus immunotherapy in the form of oral BCG given every two weeks.

**Progress:** This protocol was closed to patient entry August 1980 and was previously reported as closed. 11 patients were entered at MAMC, 8 have died, 3 are still being followed. The protocol was reactivated in December 1993 so that SWOG could continue to collect data on these patients.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 78/002		<b>Status:</b> On-going
<b>Title:</b> SWOG 7713/14: Chemoimmunotherapy in Non-Hodgkin's Lymphoma CHOP vs CHOP + Levamisole vs CHOP + Levamisole + BCG for Remission Induction Therapy: Levamisole vs No Maintenance After Remission Induction				
<b>Start Date:</b> 10/21/77		<b>Est. Completion Date:</b> Jun 79		
<b>Department:</b> SWOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC				
<b>Associate Investigators:</b> COL Friedrich H. Stutz, MC		LTC H. Irving Pierce, MC		
<b>Key Words:</b> Cancer:Non-Hodgkin's lymphoma, CHOP, Levamisole, BCG				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	11/18/94

**Study Objective:** (1) To compare the effectiveness, in terms of rate of response of two chemoimmunotherapy regimens (CHOP + levamisole vs CHOP + levamisole + BCG) against CHOP for remission induction in previously untreated patients with non-Hodgkin's lymphoma; (2) For patients proven to be in complete remission after induction, to compare the duration of documented complete response obtained by continued maintenance immunotherapy with levamisole vs no maintenance therapy; (3) For patients with impaired cardiac function (not eligible for treatment with adriamycin), with mycosis fungoides, or with only a partial response to 11 courses of treatment with levamisole + BCG, to estimate the complete response rate obtained by continued chemoimmunotherapy with COP + levamisole; (4) To estimate the CNS relapse rate in patients with diffuse lymphomas when CNS prophylaxis with intrathecal cytosine arabinoside is used; (5) To continue to evaluate the impact of systematic restaging of patients judged to be in complete remission and the value of expert hematopathology review of diagnostic material from all cases; (6) To establish baseline and serial data on immunologic status in bother chemoimmunotherapy groups.

**Technical Approach:** Patients with a diagnosis of non-Hodgkin's lymphoma established by biopsy with no prior chemotherapy are eligible. Patients with chronic lymphocytic leukemia are ineligible. Patients with preexisting cardiac disease or mycosis fungoides are ineligible for the CHOP programs, but will be treated with COP + levamisole. Patients will be stratified according to nodular or diffuse histologies, adequate or impaired bone marrow reserves, presence or absence of bone marrow involvement, and performance status. Initial drug doses are based on bone marrow reserve. Treatment plans as outlined in the protocol.

**Progress:** This protocol was closed to patient entry October 1982 and was previously reported as completed. 4 patients were entered at MAMC, 3 have died, one patient is still being followed. The protocol was reactivated in December 1993 do that SWOG could continue to collect data on these patients.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 78/047		<b>Status:</b> On-going	
<b>Title:</b> SWOG 7808: Combination Modality Treatment for Stage III and Stage IV Hodgkin's Disease, MOPP #6					
<b>Start Date:</b> 07/31/78			<b>Est. Completion Date:</b> Jan 88		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC					
<b>Associate Investigators:</b> LTC H. Irving Pierce, MC			COL Friedrich H. Stutz, MC Suresh B. Katakhar, M.D., DAC		
<b>Key Words:</b> Hodgkin's disease:Stages III & IV,chemotherapy,modality RX					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
<b>Periodic Review:</b>					12/17/93

**Study Objective:** To attempt to increase the complete remission rate induced with MOP-BAP (nitrogen mustard, vincristine, procarbazine, prednisone, adriamycin, and bleomycin) alone utilizing involved field radiotherapy in patients with Stages III and IV Hodgkin's disease achieving partial remission at the end of 6 cycles; and to determine if immunotherapy maintenance with levamisole or consolidation with low dose involved field radiotherapy will produce significantly longer remission durations over a no further treatment group when complete remission has been induced with 6 cycles of MOP-BAP in Stages III & IV Hodgkin's.

**Technical Approach:** Patients (>15 yrs) must have histologic diagnosis of Hodgkin's disease; no prior chemotherapy. Patients with a history of congestive heart failure, valvular heart disease, or serious obstructive or restrictive pulmonary disease will be excluded. Normal marrow patients will receive six cycles of MOP-BAP. Impaired bone marrow patients will receive six cycles of MOP-BAP with dose modifications. Complete Remission (CR) patients with prior radiotherapy will be randomized to Treatment 3 (no treatment) or Treatment 4 (levamisole). CR patients without prior radiotherapy will receive Treatment 5 (radiotherapy). Partial remission (PR) patients without prior radiotherapy or residual bone marrow involvement will receive Treatment 6 (radiotherapy). PR patients with prior radiotherapy or those with residual bone marrow involvement will receive Treatment 7 (4 additional cycles of MOP-BAP); after 10 total cycles of MOP-BAP, patient will continue study on MOP-BAP therapy at the discretion of the investigator.

**Progress:** This study was closed to patient entry 1 Dec 87. Thirteen patients were enrolled in previous years and 5 are still being followed.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 79/096		<b>Status:</b> On-going	
<b>Title:</b> SWOG 7827: Combined Modality Therapy for Breast Carcinoma, Phase III					
<b>Start Date:</b> 09/21/79			<b>Est. Completion Date:</b> Sep 81		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC					
<b>Associate Investigators:</b> Suresh B. Katakhar, M.D., DAC			COL Friedrich H. Stutz, MC COL Irwin B. Dabe, MC		
<b>Key Words:</b> cancer:breast,chemotherapy,modality therapy					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		12/17/93

**Study Objective:** To compare the disease-free interval and recurrence rates in: (1) estrogen receptor positive (ER+) premenopausal patients with Stage II disease using combination chemotherapy alone vs combination chemotherapy and oophorectomy; (2) ER+ postmenopausal patients with Stage II disease using combination chemotherapy plus tamoxifen vs tamoxifen alone vs combination chemotherapy alone; (3) estrogen receptor negative (ER-) patients with Stage II disease using one vs two years of combination chemotherapy; to compare the effect of adjuvant therapy in Stage II breast cancer using partial mastectomy and radiation vs modified radical or radical mastectomy; to compare the effect of the various adjunctive therapy programs upon survival patterns; and to correlate the estrogen receptor status with disease-free interval and survival.

**Technical Approach:** Patients with a histologically proven diagnosis of breast cancer (Stage II or Stage III) with one or more pathologically involved axillary nodes will receive one of the following treatments: (CMFVP = cyclophosphamide, methotrexate, 5-FU, vincristine, and prednisone): (1) CMFVP for 1yr pre- or postmenopausal ER patients. (2) CMFVP for 2 yr pre- or postmenopausal ER patients. (3) CMFVP for 1 yr premenopausal ER+ patients. (4) Oophorectomy + CMFVP premenopausal ER+ patients. (5) Tamoxifen alone for 1 yr postmenopausal ER+ patients. (6) CMFVP for 1 yr postmenopausal ER+ patients. (7) Tamoxifen + CMFVP for 1 yr postmenopausal ER+ patients. Patients undergoing segmental mastectomy (lumpectomy) will receive 6 wks of radiation therapy in addition to the treatment they are randomized to receive.

**Progress:** Thirty-five patients were enrolled prior to closure of patient enrollment 15 Aug 89. Twenty-two patients are still being followed.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 81/064		<b>Status:</b> On-going	
<b>Title:</b> SWOG 8027: The Natural History of Pathological Stage T(1-2) N(O), M(O) ER+ Breast Cancer					
<b>Start Date:</b> 03/20/81			<b>Est. Completion Date:</b> Jan 83		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC					
<b>Associate Investigators:</b> A.W. Brown			COL Irwin B. Dabe, MC		
<b>Key Words:</b> Cancer:breast, natural history					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		11/18/94	

**Study Objective:** To document recurrence rates, patterns of recurrence, and survival among patients with Stage I or Stage II node negative (T<sub>1-2</sub> N<sub>0</sub> M<sub>0</sub>) breast cancer whose tumors are determined to be estrogen receptor positive at the time of surgery.

**Technical Approach:** Patients having undergone radical, modified radical, or adequate local excision with node dissection for histologically proven breast carcinoma whose axillary nodes are negative for tumor and whose estrogen receptor status is positive are eligible. Patients undergoing local adequate excision with axillary node sampling as primary treatment must receive radiation therapy beginning 14-20 days post-operatively as outlined in the protocol. Only patients with pathologic Stage T<sub>1-2</sub> N<sub>0</sub> M<sub>0</sub> with a primary tumor of ≤5 cm are eligible. The primary tumor must be movable in relationship to the anterior chest wall and may not be involved with extensive skin ulcerations. This protocol involves no randomization or treatment. It consists only of follow-up and documentation of natural history. Patients will be stratified by primary tumor size, <2 cm vs 2 to 5 cm, and by menopausal status. Patients will be followed until relapse or for 10 years, whichever comes sooner.

**Progress:** Closed to patient entry Oct 82. Five patients were entered; three are still being followed. This protocol was previously reported as completed. In fact, patients are still being followed and the protocol was reactivated in December 1993 so that SWOG could continue to collect data on these patients.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 84/018		<b>Status:</b> On-going	
<b>Title:</b> SWOG 8216/38: Comparison of BCG Immunotherapy and Adriamycin for Superficial Bladder Cancer					
<b>Start Date:</b> 11/18/83			<b>Est. Completion Date:</b> Sep 85		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC					
<b>Associate Investigators:</b>			COL William D. Belville, MC		
COL Friedrich H. Stutz, MC			COL Irwin B. Dabe, MC		
MAJ Thomas M. Baker, MC			MAJ Alfred H. Chan, MC		
MAJ Timothy J. O'Rourke, MC			MAJ Michael D. Stone, MC		
<b>Key Words:</b> cancer:bladder,BCG,adriamycin					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	12/17/93	

**Study Objective:** To compare the effectiveness of intravesical BCG immunotherapy with intravesical Adriamycin in chemotherapy with respect to disease-free interval and two-year recurrence rate; to compare the toxicity of topical immunotherapy and chemotherapy; and to obtain experience regarding disease-free interval and the recurrence rate in patients who develop tumor recurrence and are then crossed over to the alternative treatment arm.

**Technical Approach:** Following a standard transurethral resection, patients will be stratified by the presence or absence of documented carcinoma in situ and as to prior chemotherapy and then randomized to receive BCG immunotherapy or Adriamycin chemotherapy. Patients who develop tumor recurrence following treatment will be eligible for crossover to the other treatment arm.

**Progress:** This study was closed to patient entry 20 Dec 85. Three patients were enrolled at MAMC and are still being followed.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 85/076		<b>Status:</b> On-going	
<b>Title:</b> SWOG 8269: Concurrent Chemo-Radiotherapy for Limited Small Cell Carcinoma of the Lung, Phase II					
<b>Start Date:</b> 08/23/85			<b>Est. Completion Date:</b> Jun 87		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC					
<b>Associate Investigators:</b> MAJ Michael D. Stone, MC MAJ Thomas M. Baker, MC			COL Irwin B. Dabe, MC CPT David R. Bryson, MC		
<b>Key Words:</b> Cancer:lung, small cell, radiation therapy, adriamycin, cis-platinum, cyclophosphamide, methotrexate, vincristine, VP-16					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 11/18/94

**Study Objective:** To explore the response rate with the concurrent use of radiation therapy plus chemotherapy utilizing cis-platinum, VP-16, and vincristine in limited small cell carcinoma of the lung and to observe the toxicities of this combined modality program.

**Technical Approach:** Patients will be started on chemotherapy consisting of cis-platinum, VP-16, and vincristine and concurrent radiation therapy to the primary site. After completion of radiation therapy to the chest, prophylactic cranial radiation therapy will be given. After a brief rest period, the patients will be treated with 12 more weeks of conventional chemotherapy consisting of adriamycin, cytoxan, VP-16, vincristine, and methotrexate. Patients who show a complete response will be followed. Patients with less than a complete response will be taken off study and offered alternative therapy.

**Progress:** This study was closed to patient entry March 86. It was previously reported as completed. In fact, two patients were entered and one is still being followed. The protocol was reactivated in December 1993 so that SWOG could continue to collect data on these patients.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 83/056		<b>Status:</b> On-going	
<b>Title:</b> SWOG 8294: Evaluation of Adjuvant Therapy and Biological Parameters in Node Negative Operable Female Breast Cancer (ECOG, EST-1180), Intergroup Study					
<b>Start Date:</b> 03/18/83			<b>Est. Completion Date:</b> Feb 85		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC					
<b>Associate Investigators:</b>			LTC James E. Congdon, MC		
COL Friedrich H. Stutz, MC			COL Irwin B. Dabe, MC		
MAJ Timothy J. O'Rourke, MC			MAJ Alfred H. Chan, MC		
MAJ Thomas M. Baker, MC					
<b>Key Words:</b> cancer:breast,surgery,biological parameters					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	12/17/93	

**Study Objective:** To assess the impact of short-term intensive chemotherapy with CMFP to prevent disease recurrence and prolong survival in node negative patients with any size estrogen receptor negative tumors and node negative patients with estrogen receptor positive tumors whose pathological size is >3 cm; to assess the impact of surgical procedure, estrogen receptor status, menopausal status and tumor size; to develop guidelines referable to histopathological features of node negative tumors which are reproducible and to assess their prognostic impact for disease-free survival and survival; to assess the value to CEA in predicting recurrence and survival rates; to assess the natural history of a subgroup with node negative, estrogen receptor positive small tumors (3 cm).

**Technical Approach:** Patients will have laboratory evaluations to ensure that there is no evidence of disseminated disease. They will be stratified into a number of treatment groups based on the site of tumor, estrogen receptor status, age, and menopausal status. Patients with primary tumors less than 3 cm in diameter who are estrogen receptor positive will be followed by close observation only to determine the natural history of their tumor. All other patients who have a somewhat greater likelihood of relapse will be randomized to receive either close observation only or 6 cycles of systemic chemotherapy. The chemotherapy will consist of 4 agents: cyclophosphamide, methotrexate, 5-fluorouracil, and prednisone given for six 28 day cycles. The dosage of the individual agents will be determined by body height and weight.

**Progress:** This study was closed to patient entry 15 May 88. Twelve patients were enrolled in previous years and nine continue to be followed. Three have expired.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 84/072		<b>Status:</b> Completed	
<b>Title:</b> SWOG 8312: Megestrol Acetate and Aminoglutethimide/Hydrocortisone in Sequence or in Combination as Second-Line Endocrine Therapy of Estrogen Receptor Positive Metastatic Breast Cancer, Phase III					
<b>Start Date:</b> 08/17/84			<b>Est. Completion Date:</b> Jun 86		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC					
<b>Associate Investigators:</b>			MAJ Thomas M. Baker, MC		
COL Friedrich H. Stutz, MC			COL Irwin B. Dabe, MC		
MAJ Timothy J. O'Rourke, MC			MAJ Michael D. Stone, MC		
<b>Key Words:</b> cancer:breast,endocrine therapy,megestrol acetate					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	12/17/93	

**Study Objective:** To determine whether combination hormonal therapy with aminoglutethimide and hydrocortisone plus megestrol acetate, agents thought to have different mechanisms of action, offers an improved response rate with prolonged response duration and increased patient survival over the sequential use of each agent in ER+ patients who have progressed after responding to primary hormonal treatment with tamoxifen; to assess the relative toxicities of megestrol acetate and medical adrenalectomy; and to assess the value of progesterone receptors in predicting subsequent responses to a variety of hormonal therapies.

**Technical Approach:** Patients show have had an adequate trial of tamoxifen and have achieved at least a partial response or maintained stable disease for a minimum of six months with documented disease progression and clear-cut bone scan evidence of cortical bone metastases will be randomized to: Arm I - megestrol acetate, 40 mg PO, 4 times daily given alone until there is documented evidence of disease progression; Arm II -aminoglutethimide, 250 mg PO, twice daily for two weeks, then 250 mg PO, four times daily plus hydrocortisone, 20 mg PO upon rising, 20 mg PO at 1700 hrs, and 60 mg PO at bedtime, daily for two weeks, then 10 mg PO upon rising, 10 mg PO at 1700 hrs, and 20 mg PO at bedtime; or Arm III - megestrol acetate as in Arm I plus aminoglutethimide as in Arm II plus hydrocortisone as in Arm II. An adequate trial of each arm will consist of at least eight weeks of daily therapy in the absence of documented evidence of disease progression. Patients in Arms I and II with documented progressive disease after an adequate trial will be crossed over to the other treatment arm. The only exception to crossover will be patients who develop life threatening brain, liver, or pulmonary metastases who require systemic chemotherapy. Patients randomized to Arm III will go off study at the time of disease progression.

**Progress:** This protocol was closed to patient entry Nov 90. It was previously reported as closed. However, two patient had been entered and one is still in follow-up. The protocol was reactivated in December 1993 so that SWOG could continue to collect data.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 84/059		<b>Status:</b> On-going	
<b>Title:</b> SWOG 8313: Multiple Drug Adjuvant Chemotherapy for Patients with ER Negative Stage II Carcinoma of Breast, Phase III					
<b>Start Date:</b> 05/18/84			<b>Est. Completion Date:</b> May 86		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC					
<b>Associate Investigators:</b>			COL Friedrich H. Stutz, MC		
COL Irwin B. Dabe, MC			MAJ Thomas M. Baker, MC		
MAJ Timothy J. O'Rourke, MC			MAJ Michael D. Stone, MC		
<b>Key Words:</b> cancer:breast,chemotherapy,emergency room					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		12/17/93	

**Study Objective:** To compare through a randomized prospective study the recurrence rates and disease-free intervals for postoperative axillary node positive estrogen receptor negative breast cancer patients given adjuvant therapy with either short term intense chemotherapy (FAC-M) or one year standard chemotherapy (CMFVP); to compare the effect of these two adjuvant therapies on survival; to compare the relative toxicity of the two therapies; to compare the quality of life of patients with operable breast cancer randomized to receive one year of CMFVP or a short intensive regimen of FAC-M x 4 courses; and to compare a multiple item questionnaire for assessing quality of life.

**Technical Approach:** Women who have histologically proven breast cancer with axillary lymph node metastasis and negative estrogen receptors will be entered 14-21 days post-lumpectomy or within 14-42 days post-mastectomy and randomly assigned to receive: Arm I a tapering course of oral prednisone for 6 weeks, weekly IV vincristine for 10 weeks, weekly IV methotrexate, and weekly IV 5-FU plus daily oral cyclophosphamide for a total of one year; or Arm II four cycles of adriamycin (IV day 1), cyclophosphamide (IV day 1), 5-FU (IV days 1 and 8), and methotrexate (IV day 22). Each cycle will be five weeks and total duration of therapy in this arm is approximately 20 weeks. Questionnaires to compare quality of life will be completed at 72 hours prior to chemotherapy. Added to this protocol will be a sub-study to determine the prognostic significance of circulating human mammary epithelial antigens. This will involve blood tests prior to chemotherapy and then once every three months.

**Progress:** This study was closed to patient entry 15 Jun 90. Three patients were enrolled, 2 have died and 1 continues to be followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 85/009		<b>Status:</b> On-going	
<b>Title:</b> SWOG 8410: Combination Chemotherapy of Intermediate and High-Grade Non-Hodgkin's Lymphoma with m-BACOD, Phase II					
<b>Start Date:</b> 11/16/84			<b>Est. Completion Date:</b> Oct 86		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC					
<b>Associate Investigators:</b>			COL Friedrich H. Stutz, MC		
COL Irwin B. Dabe, MC			MAJ Timothy J. O'Rourke, MC		
MAJ Michael D. Stone, MC			CPT David R. Bryson, MC		
MAJ Thomas M. Baker, MC					
<b>Key Words:</b> Cancer: Non-Hodgkin's lymphoma, m-BACOD					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	11/18/94	

**Study Objective:** To determine an approximate complete remission rate and remission duration for the treatment program of cyclophosphamide, doxorubicin, vincristine, dexamethasone, and bleomycin with intervening moderate dose of methotrexate and leucovorin rescue (m-BACOD) in patients with intermediate and high grade non-Hodgkin's lymphoma and to assess the feasibility of using this regimen in the SWOG with the intent of using m-BACOD in a future Phase III trial.

**Technical Approach:** Patients will be stratified according to marrow reserve status and creatinine clearance. Treatment will consist of ten 3-week courses. Cytosan, adriamycin, vincristine, and bleomycin will be given IV on day 1. Dexamethasone will be given by mouth daily for 5 days, and methotrexate will be given on days 8 and 15 at 200 mg/m<sup>2</sup>. Leucovorin will be given 10 mg/m<sup>2</sup> by mouth after each methotrexate injection every 6 hours for eight doses. An adequate trial will be defined as the completion of two complete cycles of m-BACOD. Patients with documented progressive disease or less than complete response after an adequate trial will be taken off study. Those with complete response will continue on study with no further chemotherapy.

**Progress:** This study was closed to patient entry April 1985 and reported as completed. However, two patients had been enrolled in the study and are still being followed. The study was reactivated in December 1993 so that SWOG could continue to collect data on these patients.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 86/007		<b>Status:</b> On-going	
<b>Title:</b> SWOG 8417/19: Evaluation of Two Consolidation Regimens in the Treatment of Adult Acute Lymphoblastic Leukemia, Phase III					
<b>Start Date:</b> 10/18/85			<b>Est. Completion Date:</b> Sep 87		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Paul C. Sowray, MC					
<b>Associate Investigators:</b>			COL Irwin B. Dabe, MC		
LTC Lauren K. Colman, MC			LTC Howard Davidson, MC		
MAJ Thomas M. Baker, MC			MAJ Michael D. Stone, MC		
CPT David R. Bryson, MC					
<b>Key Words:</b> leukemia:lymphoblastic,consolidation regimens					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		12/17/93	

**Study Objective:** To compare the effects on remission duration and survival of two consolidation regimens: the L-10-M consolidation used in SWOG 8001 versus a regimen employing daunomycin, cytosine, arabinoside, 6-thioguanine and escalating methotrexate/Lasparaginase in patients with adult lymphoblastic leukemia and to compare the toxicities of the two consolidation regimens.

**Technical Approach:** Patients will begin remission induction with vincristine, prednisone, adriamycin, methotrexate, cyclophosphamide, and adriamycin (36 days), followed by a 14 day rest period. On day 30, patients will have an Ommaya reservoir placed in the frontotemporal area of the skull. Patients failing to achieve an A1 marrow status on induction therapy will go off study. Patients with complete remission will be randomized to one of the following consolidation regimens: ARM I (L-10-M) methotrexate and Ara-c, daily x 5 on days 1, 36, and 71; Ara-c and 6-thioguanine every 12 hr for 12 doses on days 15, 50, and 85; methotrexate days 15, 17, 57, and 59; vincristine and prednisone days 50 and 57; L-asparaginase beginning day 99, three times weekly for a total of 6 doses, and cyclophosphamide day 110 following last dose of L-asparaginase. Arm II: daunomycin days 1-3, Ara-C continuous infusion days 1-5, 6-thioguanine every 12 hr days 15, followed by a 21-28 day rest period. Methotrexate every 10 days from 28-98, L-asparaginase every 10 days 29-99. After a 2-week rest period, maintenance therapy will begin with vincristine, prednisone, adriamycin, 6-mercaptopurine, methotrexate (IT), methotrexate PO, dactinomycin, vincristine, prednisone, BCNU, cyclophosphamide, 6-mercaptopurine, and methotrexate (repeated every 21 weeks for 36 months or until relapse. An adequate trial will be the completion of remission induction.

**Progress:** This study closed to patient entry 15 Jan 93. Seven patients were enrolled MAMC. All original patients enrolled at MAMC have died but 1 patient has transferred in and is being followed.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 87/033		<b>Status:</b> On-going	
<b>Title:</b> SWOG 8501 (INT 0051): Intraperitoneal Cis-platinum/IV Cyclophosphamide vs IV cis-platinum/IV Cyclophosphamide in Patients with Non-measurable (Optimal) Disease Stage III Ovarian Cancer, Phase III ....					
<b>Start Date:</b> 01/16/87			<b>Est. Completion Date:</b> Dec 89		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC					
<b>Associate Investigators:</b>			MAJ Thomas M. Baker, MC		
COL Irwin B. Dabe, MC			LTC Lauren K. Colman, MC		
MAJ David M. Dunning, MC			MAJ Ruben D. Sierra, MC		
CPT David R. Bryson, MC			COL Roger B. Lee, MC		
<b>Key Words:</b> cancer:ovarian,chemotherapy,IP,IV cyclophosphamide,cisplatinum					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	12/17/93	

**Study Objective:** To perform a Phase III randomized trial of intermediate dose intraperitoneal (IP) cis-platinum and intravenous (IV) cyclophosphamide vs intermediate dose IV cis-platinum and cyclophosphamide for optimal Stage III ovarian cancer; to evaluate the comparative toxicities of the two regimens; and to determine, in the setting of a prospective randomized trial, if the human tumor clonogenic assay with a wide range of drug concentration testing can accurately predict pathologic complete response to two-drug combination therapy in the setting of systemic and IP drug administration.

**Technical Approach:** Only patients with epithelial neoplasms will be eligible. Patients will be stratified by amount of residual disease and performance. They will be randomized to Arm I or Arm II. Arm I: IV cisplatin, 100 mg/m<sup>2</sup> plus IV cyclophosphamide, 600 mg/m<sup>2</sup> every 28 days for six courses. Arm II: IP cisplatin, 100 mg/m<sup>2</sup> plus IV cyclophosphamide, 600 mg/m<sup>2</sup>, every 28 days for six courses. Patients with partial or no response will go off study. Those with clinical complete response will undergo second look laparotomy. Those with residual tumor at second look laparotomy will be taken off study and entered in an appropriate protocol. Those with pathologic complete response will be followed by observation only until evidence of progression of disease appears. All patients who receive any amount of chemotherapy will be evaluable for toxicity. Patients who receive at least two courses of therapy will be evaluable for response and survival.

**Progress:** This study was closed to patient entry 15 Jul 92. One patient was entered in Dec 86 and refused second look surgery so he was taken off the protocol, but is being followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 87/107		<b>Status:</b> On-going	
<b>Title:</b> SWOG 8507: Maintenance versus No Maintenance BCG Immunotherapy of Superficial Bladder Cancer, Phase III					
<b>Start Date:</b> 08/21/87			<b>Est. Completion Date:</b> Aug 90		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC					
<b>Associate Investigators:</b>			COL Irwin B. Dabe, MC		
COL William D. Belville, MC			COL Victor J. Kiesling, MC		
LTC Lauren K. Colman, MC			MAJ Thomas M. Baker, MC		
MAJ David M. Dunning, MC			MAJ Ruben D. Sierra, MC		
CPT Denis Bouvier, MC					
<b>Key Words:</b> cancer:bladder,BCG,immunotherapy					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		12/17/93	

**Study Objective:** To compare the effectiveness of intravesical and percutaneous BCG immunotherapy given on a maintenance versus no maintenance schedule with respect to disease-free interval and rate of tumor recurrence in patients with transitional cell carcinoma of the bladder; to assess the toxicity of maintenance and no maintenance BCG immunotherapy; and to assess the association of intermediate strength PPD skin test reactivity with disease free status in patients treated with BCG immunotherapy.

**Technical Approach:** Patients will be stratified according to prior chemotherapy, disease type, and PPD skin test conversion. One week following a standard transurethral resection, BCG, 120 mg lyophilized BCG organisms will be diluted in 50.5 cc of sterile, preservation-free saline. Fifty cc will be administered intravesically and 0.5 cc will be administered percutaneously. The BCG administration will be repeated weekly for a total of six weeks. Patients will then be randomized to the BCG maintenance or no maintenance arms. The BCG maintenance arm will consist of weekly intravesical and percutaneous BCG immunotherapy administrations repeated for three consecutive weeks at three months, six months, and every six months thereafter for a total treatment period of 36 months. Patient removal from the study will be determined by the type of tumor. Any patient with progression of disease, defined by an increase in tumor grade or stage beyond the highest previous grade or stage or an increase in the number or frequency or recurrences will be removed from the study.

**Progress:** This study closed to patient entry 15 Dec 88. Eleven patients were entered in the study and 10 are still being followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 86/080		<b>Status:</b> On-going	
<b>Title:</b> SWOG 8516: A Phase III Comparison of CHOP versus m-BACOD versus ProMACE-CytaBOM versus MACOP-B in Patients with Intermediate or High-Grade Non-Hodgkin's Lymphoma					
<b>Start Date:</b> 08/15/86			<b>Est. Completion Date:</b> Jul 89		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC					
<b>Associate Investigators:</b> COL Irwin B. Dabe, MC MAJ David M. Dunning, MC			MAJ Thomas M. Baker, MC LTC Lauren K. Colman, MC CPT David R. Bryson, MC		
<b>Key Words:</b> lymphoma:non-Hodgkin's,chemotherapy,CHOP,m-BACOD,M					
<b>Accumulative</b> <b>MEDCASE Cost:</b>		<b>Est. Accumulative</b> <b>OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		11/18/94	

**Study Objective:** To compare in a randomized group-wide setting the complete response rate, response duration, and survival of patients with intermediate and high grade non-Hodgkin's lymphoma treated with one of four combination chemotherapy regimens: CHOP, m-BACOD, ProMACE-CytaBOM, or MACOP-B; and to compare the toxicities of each regimen in this patient population.

**Technical Approach:** Patients with prior chemotherapy or radiotherapy are ineligible. Arm I (CHOP every 3 weeks for 8 consecutive cycles): cyclophosphamide (IV), doxorubicin (IV), vincristine (IV) and prednisone (PO). Arm II (m-BACOD every 3 weeks x 10): cyclophosphamide (IV), doxorubicin (IV), vincristine (IV), bleomycin (IV), dexamethasone (PO), methotrexate (IV), and calcium Leucovorin rescue after each MTX dose. Arm III (Pro-MACE-CytaBOM every 21 days, treated until complete remission plus 2 additional cycles): cyclophosphamide (IV), doxorubicin (IV), VP-16 (IV), Prednisone(PO), Ara-C (IV), bleomycin (IV), vincristine (IV), methotrexate (IV), calcium leucovorin rescue after each MTX dose, and trimethoprim-sulfamethoxazole (PO). Arm IV (MACOP-B will be given over 12 weeks): methotrexate (IV), calcium leucovorin rescue after each MTX bolus, doxorubicin (IV), cyclophosphamide (IV), vincristine (IV), bleomycin (IV), prednisone (PO), and trimethoprim-sulfa (PO). Patients with documented progressive disease may be taken off study at any time; however patients will preferably be restaged upon completion of the treatment program to assess response. Patients with less than a complete response at restaging will be taken off study. Patients whose clinical disease has disappeared and who appear to be in complete remission will undergo a complete and thorough laboratory and radiographic search for evidence of persistent lymphoma approximately one month after completion of therapy. If complete remission is confirmed, the patient will be observed with no further therapy.

**Progress:** This study was closed to patient entry, June 1991, and was previously reported as completed. However, two patients were transferred in from another Army medical center and MAMC now follows these patients. It was reactivated in December 1993.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 85/073	<b>Status:</b> On-going
<b>Title:</b> SWOG 8590: Phase III Study to Determine the Effect of Combining Chemotherapy with Surgery and Radiotherapy for Resectable Squamous Cell Carcinoma of the Head and Neck, Phase III (Intergroup Group.....		
<b>Start Date:</b> 06/28/85	<b>Est. Completion Date:</b> May 87	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Howard Davidson, MC		
<b>Associate Investigators:</b>		
COL Friedrich H. Stutz, MC	MAJ Thomas M. Baker, MC	
COL William J. Gernon, MC	COL Irwin B. Dabe, MC	
MAJ Michael D. Stone, MC	MAJ Timothy J. O'Rourke, MC	
LTC Donald B. Blakeslee, MC	CPT David R. Bryson, MC	
<b>Key Words:</b> head & neck,surgery,chemotherapy,radiotherapy		
<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	12/17/93

**Study Objective:** To test whether the addition of chemotherapy to surgery and radiotherapy prolongs disease-free survival and survival between the two study groups; to test whether the addition of chemotherapy to surgery and radiotherapy increases local control rates at the primary site and/or the cervical neck nodes; and to determine if the patterns of failure have been changed with the addition of chemotherapy.

**Technical Approach:** After surgery, patients will be randomized to either chemotherapy plus radiation therapy or radiation therapy alone. In the chemotherapy plus radiation therapy group, the chemotherapy will start 2-4 weeks after surgery and the radiotherapy will start approximately two weeks after completing chemotherapy. In the radiation therapy alone group, the radiation therapy will begin 2-4 weeks after surgery. Chemotherapy will be cisplatinum give day 1 and 5 FU given days 1-5 and repeated every 21 days for three courses. Patients who develop local or distant recurrence following therapy will be treated at the physician's discretion.

**Progress:** This study was closed to patient entry 1 Feb 90. Three patients were entered in previous years and are still being followed.

### Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 85/064

**Status:** On-going

**Title:** SWOG 8591: NCI Intergroup #0035, An Evaluation of Levamisole Alone or Levamisole plus 5-Fluorouracil as Surgical Adjuvant Treatment for Resectable Adenocarcinoma of the Colon, Phase III - Intergroup

**Start Date:** 05/24/85

**Est. Completion Date:** Apr 87

**Department:** SWOG

**Facility:** MAMC

**Principal Investigator:** LTC Howard Davidson, MC

**Associate Investigators:**

COL Friedrich H. Stutz, MC

MAJ Jens A. Strand, MC

MAJ Michael D. Stone, MC

MAJ Thomas M. Baker, MC

COL Irwin B. Dabe, MC

MAJ Timothy J. O'Rourke, MC

CPT David R. Bryson, MC

**Key Words:** cancer:colon,levamisole,5-Fluorouracil

**Accumulative**

**MEDCASE Cost:** \$0.00

**Est. Accumulative**

**OMA Cost:** \$0.00

**Periodic Review:**

12/17/93

**Study Objective:** To assess the effectiveness of levamisole alone and levamisole plus 5-FU as surgical adjuvant regimens for resectable colon cancer; to compare each regimen to untreated controls to determine whether it yields improved survival and if it yields improved time to recurrence, with evaluations conducted independently in patients with Dukes stage B and Dukes stage C lesions.

**Technical Approach:** Patients with adenocarcinoma arising in the colon who have had a potentially curative section will be eligible. The patients with modified Dukes B2 (serosal penetration) or B3 (invasion of adjacent organs by direct extension) will be randomized to either follow-up without adjuvant therapy or adjuvant therapy with levamisole plus 5-FU. Patients with modified Dukes Stage C (involvement of regional lymph nodes) will be randomized to follow-up without adjuvant therapy, adjuvant therapy with levamisole alone, or adjuvant therapy with levamisole plus 5-FU.

**Progress:** This study was closed to patient entry 21 Oct 87. Seven patients were enrolled in previous years and 6 are still being followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 87/045		<b>Status:</b> On-going	
<b>Title:</b> SWOG 8600: A Randomized Investigation of High-Dose Versus Standard Dose Cytosine Arabinoside with Daunorubicin in Patients with Acute Non-lymphocytic Leukemia					
<b>Start Date:</b> 02/27/87			<b>Est. Completion Date:</b> Feb 90		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Paul C. Sowray, MC					
<b>Associate Investigators:</b>			COL Irwin B. Dabe, MC		
LTC Lauren K. Colman, MC			LTC Howard Davidson, MC		
MAJ Thomas M. Baker, MC			MAJ David M. Dunning, MC		
MAJ Ruben D. Sierra, MC			CPT David R. Bryson, MC		
<b>Key Words:</b> leukemia:non-lymphocytic,Ara-C,daunorubicin,cytosine arabinoside					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		12/17/93	

**Study Objective:** To compare, among patients with acute nonlymphocytic leukemia, the rate of complete remission produced by induction regimens of either standard dose cytosine arabinoside and daunorubicin or high-dose cytosine arabinoside and daunorubicin; to compare the duration of complete remission and of disease-free survival among patients who receive one of the three combinations of induction and consolidation regimens listed below; to determine the comparative toxicities of these three programs, and to determine the feasibility of implementing a predetermined approach to supportive care for these patients in a multi-institutional cooperative group setting.

**Technical Approach:** Patients will be stratified according to age and institution. Induction therapy will consist of standard dose Ara-C plus daunorubicin (Arm I) or high dose Ara-C + daunorubicin (Arm II). Patients requiring a second cycle of induction will receive the same doses as cycle 1, following the recovery of hematologic toxicities. Consolidation chemotherapy will begin when bone marrow and blood counts have recovered or on day 28 after the last induction cycle. Patients initially randomized to Arm I will be randomized to Arm III (high dose, one cycle only) or Arm IV (standard dose, two cycles). Patients initially randomized to Arm II (high dose) will be assigned to Arm III. Following the completion of consolidation, no further therapy will be given and patients will be followed only. Supportive care will include a predetermined antibiotic regimen determined by the physician.

**Progress:** This study was closed to patient entry 1 Dec 91. Of the seven patients enrolled at MAMC, 5 have died and 2 are still being followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 89/045		<b>Status:</b> Completed	
<b>Title:</b> SWOG 8621: Chemohormonal Therapy of Postmenopausal Receptor-Positive Breast Cancer, Phase III					
<b>Start Date:</b> 03/17/89			<b>Est. Completion Date:</b> Mar 92		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC					
<b>Associate Investigators:</b>			COL Irwin B. Dabe, MC		
MAJ Mark H. Kozakowski, MC			MAJ Everardo E. Cobos Jr., MC		
CPT Denis Bouvier, MC			MAJ Kenneth A. Bertram, MC		
<b>Key Words:</b> cancer:breast,postmenopausal,chemohormonal therapy					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$2316.00		12/17/93	

**Study Objective:** To compare initial combined chemo-hormonal therapy with initial hormonal therapy with respect to survival; to compare chemo-hormonal therapy using tamoxifen with that using DES with respect to survival; and to compare combined chemohormonal therapy with initial hormonal therapy with respect to response in patients with measurable disease.

**Technical Approach:** Postmenopausal females with recurrent or disseminated breast cancer, tumor positive for estrogen receptor or progesterone receptor, and adequate bone marrow and hepatic function will be eligible. Patients who have received prior hormonal therapy or chemotherapy will not be eligible. Prior adjuvant chemotherapy will be allowed if disseminated disease developed more than six months after completing adjuvant therapy, except for tamoxifen and DES. Patients with a history of deep vein thrombosis, cerebral embolus, stroke, congestive heart failure, or ischemic heart disease will not be eligible. No concurrent malignancy is allowed except for cured non-melanoma skin cancer, in situ cervical cancer, or other cancer from which the patient has been disease-free for five years. Patients will be stratified by dominant disease (osseous vs soft tissue vs visceral) and disease status. Descriptive factors will be prior adjuvant therapy; presence or absence of ascites or pleural effusions; performance status; disease free interval; number of metastatic sites, and receptor status. Patients will be randomized to: Arm I (DES); Arm II (Tamoxifen); Arm III (DES + 5-FU + cyclophosphamide + methotrexate); or Arm IV (Tamoxifen + 5-FU + cyclophosphamide + methotrexate). Patients who respond (or have prolonged disease stabilization at six months and then relapse) to tamoxifen or DES will be treated with sequential secondary and tertiary hormonal therapy if they continue to have endocrinereceptor tumors. Patients with progressive disease or short term stable disease will go off study.

**Progress:** One patient was enrolled in this study prior to closure to patient entry 1 Aug 91 and expired this FY.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 89/058		<b>Status:</b> Completed	
<b>Title:</b> SWOG 8692 (INT 0075): Therapy in Premenopausal Women with Advanced, ER Positive or PgR Positive Breast Cancer: Surgical Oophorectomy vs the LH-RH Analog, Zoladex: Phase III, Intergroup					
<b>Start Date:</b> 05/19/89			<b>Est. Completion Date:</b>		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC					
<b>Associate Investigators:</b>			COL Irwin B. Dabe, MC		
MAJ Mark H. Kozakowski, MC			MAJ Everardo E. Cobos Jr., MC		
MAJ Kenneth A. Bertram, MC			CPT Denis Bouvier, MC		
<b>Key Words:</b> cancer:breast,surgical oophorectomy,Zoladex,ER,PgR positive					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	12/17/93	

**Study Objective:** To compare the response rate, the time to treatment failure, and survival of medical castration using Zoladex to surgical castration in premenopausal women with advanced, ER+ or PgR+ breast cancer; to assess the response rate to surgical castration in patients failing to respond to or relapsing on Zoladex and the response rate to Zoladex in patients failing to respond to or relapsing on surgical castration; to compare toxicities of medical castration and surgical castration; to assess the value of post-treatment hormone levels in predicting response to medical castration; and to assess the effect of long term Zoladex treatment on hormone levels in responding patients.

**Technical Approach:** Patients must have a performance status of 02. Patients with extensive liver metastases, lymphangitic lung metastases, or prior hormone therapy or chemotherapy for advanced disease will be ineligible. Prior adjuvant chemotherapy is allowed; adjuvant tamoxifen is allowed provided relapse occurred > 6 months after completion of therapy. Patients will be stratified by disease status, dominant site of disease, performance status, and prior adjuvant tamoxifen (yes or no). Patients will be randomized to receive either surgical oophorectomy or Zoladex, 3.6 mg subcutaneously every four weeks. Surgical castration patients clearly progressing after six weeks will be crossed over to Zoladex. Patients then developing progressive disease will be taken off study. Zoladex patients with clearly progressive disease after six weeks will cross over to surgical oophorectomy. Upon development of progressive disease, patients will be removed from the study.

**Progress:** This study closed to patient entry 15 July 95. No patients were enrolled at MAMC.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 90/039	<b>Status:</b> On-going
<b>Title:</b> SWOG 8710: Trial of Cytectomy Alone Versus Neoadjuvant M-VAC + Cytectomy in Patients with Locally Advanced Bladder Cancer (INT-0080/EST-1877, CALGB-8891)		
<b>Start Date:</b> 02/16/90	<b>Est. Completion Date:</b> Mar 92	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Rodney C. Davis, MC		
<b>Associate Investigators:</b>		
MAJ Paul C. Sowray, MC	LTC Howard Davidson, MC	
MAJ Everardo E. Cobos Jr., MC	MAJ Mark H. Kozakowski, MC	
CPT Denis Bouvier, MC	MAJ Patrick L. Gomez, MC	
MAJ Robert L. Sheffler, MC	MAJ Kenneth A. Bertram, MC	
	LTC John A. Vaccaro, MC	
<b>Key Words:</b> cancer:bladder,cystectomy,M-VAC		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	12/17/93

**Study Objective:** To study insulin induced hypoglycemia as a model of acute stress and to determine if the change in testosterone seen with acute stress is related to cortisol alone or whether it can also be seen with the stimulation of other adrenal precursor products.

**Technical Approach:** Ten healthy male volunteers (18-35 years) who are without evidence of current acute or chronic illness will have an insulin tolerance test done with blood samples drawn for cortisol, testosterone, immunoactive LH, bioactive LH, estradiol, and glucose, every 15 minutes for one hour prior to the human insulin bolus to establish baseline values. Blood samples will continue to be drawn every 15 minutes for 180 minutes after injection of the insulin. SHBG will be measured on the first and last sample and endorphin levels will be measured at baseline and at times corresponding to maximal hypoglycemia. A standard multiple dose metyrapone test will be performed one month from the insulin tolerance test. Just before the first dose and four hours after the last dose, serum samples will be obtained for cortisol, estradiol, immunoactive LH, bioactive LH, testosterone, ACTH, SHBG, endorphins, and 11-deoxycortisol. The relationship of bioactive LH to immunoactive LH will be compared using the biologic to immunologic ratio both before and during the acute stress. The data from the metyrapone test will be used to determine if metyrapone can cause a decrease in serum testosterone acutely. Again, the B/I ratio will be compared pre and post-test. Changes in serum concentrations of the measured hormones will be analyzed by repeated measures analysis of variance.

**Progress:** No patients have been entered in this study at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 88/065		<b>Status:</b> On-going	
<b>Title:</b> SWOG 8736: Treatment of Localized Non-Hodgkin's Lymphoma: Comparison of Chemotherapy (CHOP) to Chemotherapy Plus Radiation Therapy					
<b>Start Date:</b> 07/15/88			<b>Est. Completion Date:</b> Jun 91		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC					
<b>Associate Investigators:</b> CPT Denis Bouvier, MC MAJ Rahul N. Dewan, MC			COL Irwin B. Dabe, MC MAJ Steven S. Wilson, MC		
<b>Key Words:</b> lymphoma:non-Hodgkin's,radiotherapy,CHOP,chemotherapy					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		12/17/93	

**Study Objective:** To evaluate, in a cooperative group setting, the difference in survival, time to treatment failure, and toxicity of two curative approaches to the treatment of patients with localized, intermediate or high grade non-Hodgkin's lymphoma.

**Technical Approach:** All patients must have biopsy proven non Hodgkin's lymphoma of intermediate or high grade histology except lymphoblastic lymphoma. Patients must have had all visible tumor removed (excisional biopsy) and must have clinically adequate liver and myocardial function to begin treatment at full doses. Patients with known central nervous system disease, previous cancer with a possibility for recurrence which might affect survival or prior chemo or radiotherapy will be ineligible. All patients will be stratified at the time of initial registration by the following: (1) age (<65 years vs >65 years); (2) Stage (I or Ie vs nonbulky II or IIe); (3) histology (diffuse large cell vs other); (4) location of disease (GI involved vs non-GI, abdominal vs non-GI, other); (5) all disease resected vs residual measurable disease. Patients will be randomized to CHOP\* (Arm I) or to CHOP plus radiation therapy (Arm II). A complete course of chemotherapy on Arm I will consist of the administration of CHOP every 21 days for eight consecutive cycles unless progressive disease develops. A complete course of chemotherapy for Arm II will consist of the administration of CHOP every 21 days for three consecutive cycles unless progressive disease develops. Radiation therapy will begin immediately after the third cycle of CHOP. Radiation therapy dose, duration, and treatment volume will be determined jointly by the radiation oncologist and the medical oncologist. All patients will be followed at three month intervals until death. CHOP: Cyclophosphamide, 750 mg/m<sup>2</sup> IV, day 1; Doxorubicin, 50 mg/m<sup>2</sup> IV, day 1; Vincristine, 1.4 mg/m<sup>2</sup> IV, day 1; Prednisone, 100 mg/day po, days 1-5.

**Progress:** Eight patients have been enrolled at MAMC (0 in FY95) and all continue to be followed. This study closed to patient entry 15 June 95.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 88/076	<b>Status:</b> On-going
<b>Title:</b> SWOG 8738: Treatment of Extensive Non-small Cell Lung Cancer: Standard Dose Cisplatin versus High-Dose Cisplatin in Hypertonic Saline Alone versus High-Dose Cisplatin/Mitomycin-C, Phase III		
<b>Start Date:</b> 09/16/88	<b>Est. Completion Date:</b> Sep 91	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Howard Davidson, MC		
<b>Associate Investigators:</b> MAJ Mark H. Kozakowski, MC MAJ Kenneth A. Bertram, MC		COL Irwin B. Dabe, MC CPT Denis Bouvier, MC
<b>Key Words:</b> cancer:lung:non-small cell,cisplatin,mitomycin-C		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 12/17/93

**Study Objective:** To compare standard dose cisplatin chemotherapy to high dose cisplatin in hypertonic saline alone to high dose cisplatin/mitomycin-C in a randomized study with stratification for known important prognostic factors with regard to response rate, response duration, and survival duration; and to compare the relative toxicities of these three chemotherapy regimens in patients with extensive non-small cell lung cancer.

**Technical Approach:** Patients will be randomized to one of the following arms: Arm I: standard dose cisplatin (50 mg/m<sup>2</sup>, IV) every four weeks for a maximum of eight cycles; ARM II: high dose cisplatin alone (100 mg/m<sup>2</sup>, IV) every four weeks for a maximum of four cycles; ARM III: high dose cisplatin (100 mg/m<sup>2</sup> IV) plus mitomycin-C (8 mg/m<sup>2</sup> IV) given every four weeks for a maximum of four cycles. All patients will have an initial assessment of response after two cycles and then reassessment after four cycles of therapy. Patients on Arm I who respond to treatment may receive continued therapy to a maximum of eight cycles. Upon progression of disease, unacceptable toxicity, or patient request, patients will be taken off treatment. All patients will be followed until death.

**Progress:** This study was closed to patient entry 1 Jun 90. Six patients were enrolled at MAMC in previous years and 2 continue to be followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 90/063		<b>Status:</b> On-going	
<b>Title:</b> SWOG 8789: A Randomized Study of Etoposide + Cisplatin and Etoposide + Carboplatin (CBDCA) in the Management of Good Risk Patients With Advanced Germ Cell Tumors					
<b>Start Date:</b> 04/20/90			<b>Est. Completion Date:</b> Apr 93		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Paul C. Sowray, MC					
<b>Associate Investigators:</b>			LTC Howard Davidson, MC		
MAJ Mark H. Kozakowski, MC			MAJ Everardo E. Cobos Jr., MC		
MAJ Patrick L. Gomez, MC			CPT Denis Bouvier, MC		
MAJ Kenneth A. Bertram, MC			MAJ Robert L. Sheffler, MC		
<b>Key Words:</b> tumor:germ cell,etoposide,cisplatin,carboplatin,CBDCA					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		12/17/93	

**Study Objective:** To determine in a randomized trial the differences in response, toxicity, time to relapse, and survival between two active chemotherapy regimens; etoposide + cisplatin and etoposide + carboplatin, for good risk patients with germ cell tumors.

**Technical Approach:** Patients with active advanced Stage II or Stage III testicular nonseminomatous germ cell tumor with a probability of complete response of >0.5 will be eligible. Patients will be randomized to Treatment Arm A (carboplatin + etoposide, given every 28 days for four cycles) or Treatment Arm B (cisplatin + etoposide every 21 days for four cycles). Following completion of chemotherapy, a complete assessment of all sites of disease will be performed. Following completion of four cycles of chemotherapy and radiographic and marker assessment, surgical resection of all residual masses will be done if deemed necessary by the principal investigator. If no residual malignant tumor or only mature teratoma is completely resected at surgery, no further therapy will be administered. If residual malignant tumor is found but is completely excised, then two more cycles of treatment will be administered. If residual malignant tumor is found but is unresectable, then the patient will receive additional therapy with standard GCT regimens or other therapy as may be indicated at the discretion of the treating physician.

**Progress:** This study closed to patient entry 15 Dec 90. One patient was enrolled at MAMC and is still being followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/119		<b>Status:</b> On-going	
<b>Title:</b> SWOG 8794: Treatment of Pathologic Stage C Carcinoma of the Prostate With Adjuvant Radiotherapy					
<b>Start Date:</b> 06/03/94			<b>Est. Completion Date:</b> Jun 98		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ J. Brantley Thrasher, MC					
<b>Associate Investigators:</b>					
COL John C. Norbeck, MC			COL John N. Wettlaufer, MC		
			MAJ Kurt L. Hansberry, MC		
CPT Bradley F. Schwartz, MC			CPT Michael D. Bagg, MC		
LTC Howard Davidson, MC			LTC Luke M. Stapleton, MC		
MAJ Patrick L. Gomez, MC			MAJ Kenneth A. Bertram, MC		
			MAJ Timothy P. Rearden, MC		
<b>Key Words:</b> Cancer:prostate, radiotherapy					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		/ /	

**Study Objective:** 1) To compare in a randomized study, the disease-free survival rates in completely resected patients with pathologic Stage C (T3N0M0) carcinoma of the prostate assigned to be treated with adjuvant external beam radiotherapy to that in patients assigned to receive no adjuvant therapy. 2) To assess the qualitative and quantitative toxicities of patients with pathologic Stage C (T3N0M0) carcinoma of the prostate when treated with external beam radiotherapy.

**Technical Approach:** Patients who have undergone radical prostatectomy and pelvic lymphadenectomy for clinical Stage A or B disease with a histologically proven diagnosis of pathologic Stage C (T3N0M0) carcinoma of the prostate will be randomized to receive either postoperative adjuvant radiation therapy (ARM I) or no adjuvant therapy (ARM II). The studies primary objective is to determine whether adjuvant radiation therapy has an effect on local control of the cancer and cancer-specific survival.

**Progress:** One patient was enrolled at MAMC and continues to be followed. Patient accrual continues.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 88/066		<b>Status:</b> On-going	
<b>Title:</b> SWOG 8796: Combination Chemotherapy for Advanced Hodgkin's Disease, Phase III Intergroup (INT 0074)					
<b>Start Date:</b> 07/15/88			<b>Est. Completion Date:</b> Jun 91		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC					
<b>Associate Investigators:</b> CPT Denis Bouvier, MC			COL Irwin B. Dabe, MC		
<b>Key Words:</b> Hodgkin's Disease,chemotherapy					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 12/17/93

**Study Objective:** To compare the effectiveness of the MOPP/ABV hybrid with sequential MOPP---->ABVD in patients with advanced or recurrent Hodgkin's disease and to determine which regimen is superior with respect to the following parameters: complete response rate, duration of complete response, freedom from progression, and survival.

**Technical Approach:** Patients must have histologic confirmation of Hodgkin's disease with no prior chemotherapy. Patients will be stratified according to age, prior radiotherapy, bulky disease, and performance status. They will then be randomized to MOPP repeated every 28 days for 6 cycles (Arm I) or to MOPP/ABV Hybrid repeated every 28 days for six cycles (Arm II). Patients on Arm I with a complete response will go on to ABVD repeated every 35 days for three cycles. Those with partial response will receive two MOPP cycles and then go on to ABVD for three cycles. Those with no change will go off study. Those patients on Arm II with complete response will receive two more cycles of MOPP/ABV. Those with partial response will continue MOPP/ABV to complete response or until a maximum of 12 cycles. Those with no change will be taken off study. MOPP: Nitrogen mustard, 6 mg/m<sup>2</sup> IV, days 1 and 8, Vincristine, 1.4 mg/m<sup>2</sup> IV, days 1 and 8, Procarbazine, 100 mg/m<sup>2</sup> PO per day x 14 days, Prednisone 40 mg/m<sup>2</sup> PO per day x 14 days. ABVD: Adriamycin, 25 mg/m<sup>2</sup> IV, days 1 and 15, Bleomycin, 10 units/m<sup>2</sup> IV, days 1 and 15, Vinblastine, 6 mg/m<sup>2</sup> IV days 1 and 15, DTIC, 375 mg/m<sup>2</sup> IV, days 1 and 15. The MOPP/ABV hybrid consist of the MOPP regimen plus adriamycin, 35 mg/m<sup>2</sup> IV, day 8; bleomycin, 10 units/m<sup>2</sup> IV day 8; and vinblastine, 6 mg/m<sup>2</sup> IV, day 8.

**Progress:** This study was closed to patient entry 1 Aug 89. One patient was enrolled at MAMC (FY88) and is still being followed.

## Detail Summary Sheet

**Date:** 30 Sep 95**Protocol No.:** 93/165**Status:** Completed**Title:** SWOG 8807: An Investigation of the Relationship Between an Integrated, System Education Approach and Breast Self Exam (BSE) Compliance, Phase III**Start Date:** 09/03/93**Est. Completion Date:** Sep 98**Department:** SWOG**Facility:** MAMC**Principal Investigator:** MAJ Timothy P. Reardon, MC**Associate Investigators:**

LTC Howard Davidson, MC

MAJ Patrick L. Gomez, MC

MAJ Robert B. Ellis, MC

CPT James S. D. Hu, MC

CPT Diana S. Willadsen, MC

LTC Luke M. Stapleton, MC

MAJ Kenneth A. Bertram, MC

MAJ Mark E. Robson, MC

MAJ Richard C. Tenglin, MC

LTC Robert D. Vallion, MC

CPT John R. Caton, MC

**Key Words:** cancer:breast, self exam**Accumulative****MEDCASE Cost:** \$0.00**Est. Accumulative****OMA Cost:** \$0.00**Periodic Review:**

12/17/93

**Study Objective:** This is a short-term randomized Phase III cancer control study to compare three educational approaches for teaching breast self exam (BSE) to healthy women who do not have learning disabilities.

**Technical Approach:** Healthy women, 20-65 years, with no history of breast cancer and consenting to participate will be administered the Intake Compliance Measurement Evaluation, scheduled for a six month follow-up visit, and told they will receive a phone contact at six and 12 months. They will then be randomized to one of three arms. ARM I participants will receive BSE instruction by physician only; ARM II will receive physician instruction + BSE class by a registered nurse; ARM III will receive physician instruction + BSE class + reinforcements in the form of calendar sticker, phone calls and monthly follow-up reminders. All BSE participants will receive a packet of educational material and be able to demonstrate a knowledge of the steps/methods for effective BSE.

Accuracy and frequency of BSE will be evaluated at six months. The Compliance Measurement Evaluation will again be administered and the participant will be asked to demonstrate BSE on the breast plate model. Twelve month follow up will be conducted by phone to determine accuracy and frequency (utilizing the Compliance Measurement form). All data will be submitted to the SWOG statistical center.

**Progress:** This study was closed to patient entry, 15 Nov 93. Approximately 25 patients were enrolled at MAMC. All 25 patients have completed 12 month follow-up. Data was submitted to SWOG for analysis.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 90/064	<b>Status:</b> On-going
<b>Title:</b> SWOG 8809: A Phase III Study of Alpha-Interferon Consolidation Following Intensive Chemotherapy with ProMACE-MOPP (Day 1-8) in Patients with Low Grade Malignant Lymphomas		
<b>Start Date:</b> 04/20/90	<b>Est. Completion Date:</b> Apr 94	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Paul C. Sowray, MC		
<b>Associate Investigators:</b>		
MAJ Mark H. Kozakowski, MC	LTC Howard Davidson, MC	
MAJ Patrick L. Gomez, MC	MAJ Everardo E. Cobos Jr., MC	
MAJ Kenneth A. Bertram, MC	CPT Denis Bouvier, MC	
	MAJ Robert L. Sheffler, MC	
<b>Key Words:</b> lymphoma,alpha-interferon,ProMACE-Mopp,chemo		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 12/17/93

**Study Objective:** To compare the disease-free survival of patients with low grade malignant lymphoma who receive alpha-interferon consolidation therapy after intensive induction with chemotherapy, with or without radiation therapy, to those who receive induction therapy alone; to determine the complete response rate, response duration, and survival of low grade lymphoma patients treated with ProMACE-MOPP; and to compare the toxicities of induction and induction plus consolidation therapy in this patient population.

**Technical Approach:** Patients must have biopsy proven, measurable, Stage III or IV non-Hodgkin's lymphoma of low grade histology. Patients will receive 6 cycles of induction chemotherapy (ProMACEMOPP, days 1-8) unless progressive disease develops during this treatment. At the completion of induction therapy, patients will be restaged to assess response. Patients whose clinical disease has disappeared and who appear to be in complete remission will undergo a complete radiographic and laboratory evaluation for evidence of persistent lymphoma approximately one month after completion of chemotherapy. If no evidence of disease is found these patients will be randomized to Alpha IFN or observation. Patients in partial response and whose bone marrow remains positive after 6 cycles of induction chemotherapy will receive 2 additional cycles of chemotherapy and then be reevaluated. If the bone marrow remains involved or the patient has less than a partial response after a total of 8 cycles, the patient will be removed from further protocol therapy. If after 8 cycles, the bone marrow is negative and the patient is in partial response, the patient will receive radiotherapy. Complete responders after induction chemotherapy; complete responders after induction chemotherapy plus radiation therapy; and partial responders after chemotherapy plus radiation therapy will be randomized to consolidation alpha interferon or observation, approximately one month after completion of therapy.

**Progress:** Four patients have been entered at MAMC (0 in FY95). All patients are still being followed. Patient accrual continues.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 89/065	<b>Status:</b> Completed
<b>Title:</b> SWOG 8812: Treatment of Limited Small Cell Lung Cancer With Concurrent Chemotherapy, Radiotherapy, With or Without GM-CSF and Subsequent Randomization To Maintenance Interferon or No Maintenance		
<b>Start Date:</b> 06/16/89	<b>Est. Completion Date:</b> Jun 92	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Paul C. Sowray, MC		
<b>Associate Investigators:</b>		
LTC Howard Davidson, MC	COL Irwin B. Dabe, MC	
MAJ Kenneth A. Bertram, MC	MAJ Everardo E. Cobos Jr., MC	
MAJ Mark H. Kozakowski, MC	CPT Denis Bouvier, MC	
<b>Key Words:</b> cancer:lung:small cell,chemo,radiotherapy,GM-CSF,interferon		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 12/17/93

**Study Objective:** To compare the days of neutropenia, the days of leukopenia, the incidence and severity of infections, the incidence and duration of fever, the days on antibiotics, and the days of hospitalization between patients receiving GM-CSF and those not receiving it; to evaluate the toxicities of GM-CSF; to evaluate the ability of rHuIFN a2 a to prolong remission duration and survival; and to evaluate the toxicities of rHuIFN a2 a.

**Technical Approach:** Patients must have histologically proven small cell carcinoma of the lung. Prior to treatment patients will be staged as to the extent of disease. Only patients with limited disease are eligible for this study. Patients must have evaluable or measurable disease, a pretreatment WBC >4,000 ml, absolute granulocyte count >1500 ml, platelet count >100,000/ ml, serum creatinine of <2.0 mg%, creatinine clearance of >50 ml/min, and performance state of 0-2 by SWOG criteria. Pregnant patients or those with prior radiation therapy, chemotherapy, colony stimulating factors, or interferon are not eligible. Patients with malignant pericardial or pleural effusions, a past medical history of congestive heart failure, extensive pulmonary disease, poor pulmonary reserve, or a history of seizures are ineligible. Patients will be stratified at initial registration by institution and at second registration according to performance status (0-1 vs 2); sex; response; and induction arm. Patients will be randomized to receive induction chemotherapy (cis-platinum + VP-16) and concurrent chest radiotherapy with or without GM-CSF. Consolidation chemotherapy will be as in induction but with no radiotherapy. Those patients achieving a complete remission will be randomized to receive or not receive maintenance therapy with recombinant alpha interferon. All patients who have achieved a complete response by week 33 will receive prophylactic cranial irradiation to the brain. Patients with stable disease, progression, or relapse at any point will be taken off study.

**Progress:** This study closed to patient enrollment 1 Jan 92. Three patients were enrolled at MAMC, all three are deceased.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 89/080		<b>Status:</b> On-going	
<b>Title:</b> SWOG 8814 (ECOG 4188, NCCTG 883051): Phase III Comparison of Adjuvant Chemoendocrine Therapy with CAF and Concurrent or Delayed Tamoxifen to Tamoxifen Alone in Postmenopausal Patients with Breast....					
<b>Start Date:</b> 09/15/89			<b>Est. Completion Date:</b> Sep 99		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC					
<b>Associate Investigators:</b>			MAJ Paul C. Sowray, MC		
MAJ Mark H. Kozakowski, MC			MAJ Everardo E. Cobos Jr., MC		
MAJ Patrick L. Gomez, MC			CPT Denis Bouvier, MC		
MAJ Kenneth A. Bertram, MC			MAJ Robert L. Sheffler, MC		
<b>Key Words:</b> cancer:breast,chemoendocrine therapy,CAF,tamoxifen					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$8692.00		12/17/93	

**Study Objective:** To compare disease-free survival and overall survival of postmenopausal primary breast cancer patients with involved axillary nodes and positive estrogen and/or progesterone receptors treated with standard adjuvant therapy with long-term Tamoxifen or with chemoendocrine therapy with CAF, followed by long-term Tamoxifen or with concurrent chemoendocrine therapy with Tamoxifen and CAF and to compare the relative toxicity of the three therapies.

**Technical Approach:** Tumors must be pathologic stage T1, T2, or T3; N; MO (Stage II or selected Stage IIIA). Patients must have histologically proven adenocarcinoma of the breast with at least one positive lymph node (tumor and/or nodes must not be fixed). Patients must have undergone a radical, modified radical, or breast sparing procedure plus axillary dissection (level I or level II). Patients with bilateral breast cancer are ineligible. Estrogen and progesterone receptors must be assayed and one and/ or the other must be positive by the institutional laboratory standards of >10 fmol/mg protein. Prestudy studies must reveal no evidence of metastatic disease. Prior hormonal or chemotherapy is not allowed and prior postmenopausal estrogen therapy is allowed but must be discontinued before registration. Stratification factors will include: involved nodes (1-3, >4); PgR+ (ER positive or negative) vs PgR(ER positive); time from surgery to randomization (<6 vs >6 weeks). Patients will be randomized to one of three treatment arms: Arm I: Tamoxifen x 5 years, Arm II: Intermittent CAF x 6 courses followed by Tamoxifen x 5 years, Arm III: Intermittent CAF x 6 courses with concurrent Tamoxifen x 5 years.

**Progress:** Seven patients have been entered in this study at MAMC (0 in FY95). All are still being followed. This study closed to patient entry 1 Aug 95.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 91/020	<b>Status:</b> On-going
<b>Title:</b> SWOG 8816: Study of 13-cis Retinoic Acid (Accutane) Plus Interferon-A (Roferon-A) in Mycosis Fungoides, Phase II		
<b>Start Date:</b> 12/07/90	<b>Est. Completion Date:</b>	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Paul C. Sowray, MC		
<b>Associate Investigators:</b>		
LTC Luke M. Stapleton, MC	MAJ William A. Phillips	
MAJ Patrick L. Gomez, MC	MAJ Everardo E. Cobos Jr., MC	
MAJ Robert L. Sheffler, MC	MAJ Kenneth A. Bertram, MC	
CPT Jennifer L. Cadiz, MC	MAJ Robert B. Ellis, MC	
<b>Key Words:</b> mycosis fungoides,retinoic acid,interferon-A		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	12/17/93

**Study Objective:** To evaluate the response rate of mycosis fungoides treated with the drug combination of 13-cis retinoic acid (Accutane) plus alpha interferon (Roferon-A) and to assess the qualitative and quantitative toxicities of the regimen in a phase II study.

**Technical Approach:** Mycosis fungoides is an uncommon lymphoma manifesting initially with skin presentation, but the disease is felt to be incurable. The regimen will be 13-cis retinoic acid, 1.0 mg/kg/day, po in two divided doses (plus vitamin E, 400 IU/day) and alpha interferon,  $3 \times 10^6$  microgm/m<sup>2</sup> subcutaneously, three times per week. After eight weeks of treatment, patients with progressive disease will go off treatment. Patients with stable disease or partial or complete remission will be treated for eight more weeks. At this point, patients who have not demonstrated a partial response will be taken off study. Patients who have partial or complete response will be treated for an additional one (complete response) or two years (partial response).

**Progress:** This study closed to patient entry 3 Jan 93. One patient was enrolled in FY92 and is still being followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 91/087	<b>Status:</b> On-going
<b>Title:</b> SWOG 8819: Central Lymphoma Repository Tissue Procurement Protocol; Companion Protocol to SWOG Studies: 8516, 8736, 8809, 8907, and 8954		
<b>Start Date:</b> 08/02/91	<b>Est. Completion Date:</b> Aug 95	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Paul C. Sowray, MC		
<b>Associate Investigators:</b>		
LTC Luke M. Stapleton, MC	LTC Howard Davidson, MC	
MAJ Everardo E. Cobos Jr., MC	MAJ Patrick L. Gomez, MC	
MAJ Robert B. Ellis, MC	MAJ Robert L. Sheffler, MC	
CPT Jennifer L. Cadiz, MC	MAJ Richard C. Tenglin, MC	
MAJ Kenneth A. Bertram, MC	CPT James S. D. Hu, MC	
<b>Key Words:</b> lymphoma:tissue procurement		
<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	12/17/93

**Study Objective:** To acquire fresh snap-frozen lymphoma tissue to establish a central lymphoma tissue repository; to establish a standard set of procedures for routine acquisition, banking, and study of lymphoma tissues within the cooperative group; to use repository tissue to establish clinical correlations via presently activated phenotyping studies and future projected molecular studies assessing specimen DNA and RNA status; and to determine if pretreatment phenotype or genotype predict patient outcome with respect to complete response rate, time to progression, and survival using prospective trial designs.

**Technical Approach:** Patients will be treated according to guidelines outlined in the specific SWOG studies. Treatment decisions will not be based on findings of the Central Lymphoma Laboratory, although clinical variables will be correlated with laboratory findings. The tissue samples will be taken from the pretreatment diagnostic biopsy or rebiopsy based on clinical decisions. Fresh biopsies (from any organ site) will be snap-frozen and submitted with one stained (hematoxylin and eosin) histologic section with accompanying pathology report. The H&E stained slide and report will accommodate morphologic correlation with immunologic findings. Tissue section analysis will be performed at the University of Arizona using three stage immunohistochemistry. Future molecular studies entailing hybridization studies of RNA and DNA fragments using DNA probes will be performed as outlined in future protocols.

**Progress:** This is a companion study using tissue from other SWOG protocols. Thus far 3 samples have been collected (0 in FY95).

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 90/027	<b>Status:</b> On-going
<b>Title:</b> SWOG 8851 (EST 5811, INT-0101): Phase III Comparison of Combination Chemotherapy (CAF) and Chemohormonal Therapy (CAF + Zoladex or CAF + Zoladex + Tamoxifen) in Premenopausal Women with Axillary....		
<b>Start Date:</b> 01/19/90	<b>Est. Completion Date:</b> Dec 99	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Howard Davidson, MC		
<b>Associate Investigators:</b>		MAJ Paul C. Sowray, MC
MAJ Mark H. Kozakowski, MC		MAJ Everardo E. Cobos Jr., MC
MAJ Patrick L. Gomez, MC		CPT Denis Bouvier, MC
MAJ Kenneth A. Bertram, MC		MAJ Robert L. Sheffler, MC
<b>Key Words:</b> cancer:breast,chemotherapy,chemohormonal therapy,premenopausal		
<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$8200.00	12/17/93

**Study Objective:** To compare the recurrence rates, disease-free intervals, relative toxicities, and hormone-receptor-positive survival for premenopausal women with axillary lymph node-positive breast cancer given adjuvant therapy with combination chemotherapy using cyclophosphamide, doxorubicin, and 5-FU (CAF) alone or CAF followed by Zoladex, or CAF followed by Zoladex plus Tamoxifen; and to assess the effect of CAF, CAF plus Zoladex, and CAF plus Zoladex and Tamoxifen on hormone levels (LH, FSH, and estradiol) in these patients.

**Technical Approach:** Patients will be nonpregnant females who have undergone excision of the primary breast tumor mass, proven histologically to be invasive breast adenocarcinoma and must have one or more pathologically involved axillary nodes. Patients who undergo total mastectomy may receive post-operative radiotherapy at the discretion of the investigator. Patients who have had prior hormonal therapy or chemotherapy for breast cancer are ineligible. Patients will be randomized to CAF alone for six cycles or to CAF for 6 cycles followed by monthly Zoladex for 5 years, or to CAF for 6 cycles followed by daily Tamoxifen and monthly Zoladex for 5 years. Adjuvant therapy will be instituted as soon as possible after mastectomy or lumpectomy. The interval between definitive surgery and initiation of adjuvant chemotherapy will not be >12 weeks. When planned, radiation therapy may be administered prior to or after (within 4 weeks of) completion of 6 cycles of adjuvant chemotherapy.

**Progress:** Six patients have been enrolled at MAMC in previous years. One patient has been lost to follow-up, five are still being followed. This study closed to patient entry 1 Feb 94.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 90/047		<b>Status:</b> On-going
<b>Title:</b> SWOG 8854: prognostic Value of Cytometry Measurements of Breast Cancer DNA from Postmenopausal Patients with Involved Nodes and Receptor Positive Tumors: A Companion Protocol to SWOG 8814				
<b>Start Date:</b> 03/16/90		<b>Est. Completion Date:</b> Mar 98		
<b>Department:</b> SWOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> cancer:breast,DNA,cytometry,postmenopausal				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	12/17/93

**Study Objective:** To determine if ploidy analysis of breast cancer by routine clinical flow cytometry (CFM) technique can predict response to therapy and survival of patients registered to SWOG 8814 and to determine if ploidy analysis by image processing technique more accurately predicts patient response to therapy and survival than ploidy analysis by flow cytometry.

**Technical Approach:** Two paraffin blocks, one representing the highest grade region of the primary tumor, the second representing the highest grade regional metastasis in a positive lymph node, will be used. From each of these blocks, two to five sections will be cut and a nuclear suspension prepared. From each suspension, a cytospin preparation will be prepared and stained with Dif-Quik to ensure that the cells present in the H & E slide are represented adequately in the nuclear preparation. A second cytospin preparation will be prepared for staining by the Feulgen technique for image processing DNA analysis. The remainder of the nuclear preparation will be stained with propidium iodide following RNase digestion for FCM DNA analysis. Cox regression modeling will be used to explore the prognostic value of ploidy status as determined by FCM and by image processing, in conjunction with the covariates tumor size, age, ER and PgR levels, and number of nodes.

**Progress:** This is a companion study using tissue from SWOG 8814. Six samples have been studied (0 in FY 95). This study closed to patient entry 15 Feb 95.

## Detail Summary Sheet

**Date:** 30 Sep 95**Protocol No.:** 91/067**Status:** On-going**Title:** SWOG 8855: Prognostic Value of Cytometry Measurements of Cellular DNA Parameters in Locally Advanced, Previously Untreated Head and Neck Cancer Patients**Start Date:** 06/14/91**Est. Completion Date:****Department:** SWOG**Facility:** MAMC**Principal Investigator:** MAJ Patrick L. Gomez, MC**Associate Investigators:**MAJ Paul C. Sowray, MC  
MAJ Robert L. Sheffler, MC  
CPT Jennifer L. Cadiz, MCLTC Howard Davidson, MC  
MAJ Everardo E. Cobos Jr., MC  
MAJ Robert B. Ellis, MC**Key Words:** cancer:head & neck,cytometry,DNA**Accumulative****MEDCASE Cost:** \$0.00**Est. Accumulative****OMA Cost:** \$0.00**Periodic Review:**

12/17/93

**Study Objective:** To evaluate the prognostic value of cellular DNA parameters of degree of DNA aneuploidy (DNA index) and proliferative activity (SPF) in predicting treatment response, time to treatment failure, and survival in patients with squamous cell carcinoma of the head and neck treated initially with cytotoxic therapy and to assess the correlation of DNA index and SPF with other patient clinical characteristics.

**Technical Approach:** Squamous cell cancers of the head and neck display a high degree of responsiveness to chemotherapy and/or radiotherapy, but a significant minority are exquisitely resistant to these treatment modalities. This will be a companion study to all SWOG head and neck cancer protocols utilizing chemotherapy as initial treatment and will use the patients registered on those studies. This study will use flow cytometrically determined cellular parameters, particularly cellular DNA content, to help identify prognostic outcome in this group of tumors. Specimens will be obtained at the time of biopsy for diagnosis, at completion of therapy if the tumor persists, or if a biopsy is performed to confirm a clinical complete response or document recurrence. All resected specimens will be sent for flow cytometry analysis. The degree of DNA aneuploidy (DNA index) and proliferative activity (SPF) will be determined by flow cytometry. These measurements will be correlated with the clinical characteristics of the patient at the time of biopsy to help predict treatment response, time to treatment failure, and survival in patients with squamous cell carcinoma of the head and neck.

**Progress:** Three patients have entered this study at MAMC in FY95. Patient accrual continues.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 90/055	<b>Status:</b> On-going
<b>Title:</b> SWOG 8892 (EST 2388, RTOG 8817, INT 0099): A Study of Radiotherapy with or without Concurrent Cisplatin in Patients with Nasopharyngeal Cancer, Phase III		
<b>Start Date:</b> 03/16/90	<b>Est. Completion Date:</b> Mar 93	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Patrick L. Gomez, MC		
<b>Associate Investigators:</b>		
MAJ Paul C. Sowray, MC	LTC Howard Davidson, MC	
MAJ Everardo E. Cobos Jr., MC	MAJ Mark H. Kozakowski, MC	
MAJ Kenneth A. Bertram, MC	CPT Denis Bouvier, MC	
MAJ Michael R. Morris, MC	MAJ Robert L. Sheffler, MC	
<b>Key Words:</b> cancer:nasopharyngeal,5-Fluorouracil,cisplatin,radiotherapy		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$3900.00	12/17/93

**Study Objective:** To compare radiotherapy with radiotherapy and concurrent cisplatin, followed by three courses of 5-FU + cisplatin for complete response rate, time to treatment failure, overall survival, pattern of recurrence, and qualitative and quantitative toxicities.

**Technical Approach:** To be eligible, patients must have histologically proven nasopharyngeal carcinoma (excluding adenocarcinoma), Stage III or IV with no evidence of distant metastatic disease, and must not be eligible for higher priority SWOG studies. Patients will be randomized as follows: Arm I: radiation therapy alone for approximately 7 weeks; Arm II: 3 courses of cisplatin (days 1, 22, and 43) concurrent with radiotherapy followed by three courses of 5-FU + cisplatin. Measurable disease must be assessed at least every eight weeks the first year of follow-up. Patients will be seen in follow-up every two months the second year, every three months the third year, and every four months thereafter. A tumor biopsy for flow cytometry will be obtained if tumor recurs.

**Progress:** One patient was enrolled in FY91 and is still being followed.



### Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 90/086

**Status:** On-going

**Title:** SWOG 8894: (INT-0105, EST-2889): A Comparison of Bilateral Orchiectomy with or without Flutamide for the Treatment of Patients with Histologically Confirmed Stage D2 Cancer

**Start Date:** 06/15/90

**Est. Completion Date:** Apr 93

**Department:** SWOG

**Facility:** MAMC

**Principal Investigator:** LTC Howard Davidson, MC

**Associate Investigators:**

MAJ Mark H. Kozakowski, MC

MAJ Patrick L. Gomez, MC

MAJ Kenneth A. Bertram, MC

LTC John A. Vaccaro, MC

MAJ Paul C. Sowray, MC

MAJ Everardo E. Cobos Jr., MC

CPT Denis Bouvier, MC

MAJ Robert L. Sheffler, MC

**Key Words:** cancer:prostate,orchiectomy,flutamide

**Accumulative**

**MEDCASE Cost:** \$0.00

**Est. Accumulative**

**OMA Cost:** \$0.00

**Periodic Review:**

12/17/93

**Study Objective:** To compare survival, progression free survival, and qualitative and quantitative toxicities between patients with orchiectomy alone and patients with orchiectomy plus Flutamide.

**Technical Approach:** Patients must have a histologically proven diagnosis of pathologic stage D2 adenocarcinoma of the prostate with evidence of metastatic disease. Patients must not have had prior hormonal therapy, chemotherapy, or biological response modifiers. Patients will be randomized to bilateral orchiectomy plus placebo po three times a day with meals or to bilateral orchiectomy plus Flutamide po three times a day with meals. Upon disease progression, patient treatment will be unblinded. Patients treated with Flutamide will be taken off protocol. Patients treated with placebo will be offered flutamide given according to the protocol guidelines until the next evidence of progression at which time they will be taken off study.

**Progress:** This study was closed to patient entry, 15 Sep 94. Three patients were enrolled at MAMC and one patient was accepted in transfer, two patients are deceased and the other two continue to be followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 90/029	<b>Status:</b> On-going
<b>Title:</b> SWOG 8897 (EST-2188, CALGB-8897, INT-0101): Phase III Comparison of Adjuvant Chemotherapy With or Without Endocrine Therapy in High-Risk, Node Negative Breast Cancer Patients, and a Natural History...		
<b>Start Date:</b> 01/19/90	<b>Est. Completion Date:</b> Jan 93	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Howard Davidson, MC		
<b>Associate Investigators:</b>		
MAJ Mark H. Kozakowski, MC	MAJ Paul C. Sowray, MC	
MAJ Patrick L. Gomez, MC	MAJ Everardo E. Cobos Jr., MC	
MAJ Kenneth A. Bertram, MC	CPT Denis Bouvier, MC	
	MAJ Robert L. Sheffler, MC	
<b>Key Words:</b> cancer:breast,chemotherapy,endocrine therapy		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$5000.00	<b>Periodic Review:</b> 12/17/93

**Study Objective:** To compare disease-free survival and overall survival of high risk primary breast cancer patients with negative axillary lymph nodes treated with standard adjuvant chemotherapy for 6 cycles; either CMF (cyclophosphamide, methotrexate, 5-FU) or CAF (cyclophosphamide, adriamycin, 5-FU); to assess the value of the addition of tamoxifen for five years compared to no tamoxifen in these patients; to compare the toxicity of the therapies; to assess the prognostic significance of DNA flow cytometry in patients with small, occult invasive breast cancer treated by local therapy only; and to evaluate the disease-free survival and survival of low risk invasive breast cancer patients determined by receptor status, tumor size, and % S phase treated by local therapy only.

**Technical Approach:** Patients must have undergone a radical, modified radical, or breast sparing procedure plus level 1 and 2 axillary lymph node dissection. Patients with bilateral breast cancer, prior hormonal or chemotherapy, or previous or concurrent malignancy are ineligible. Low risk patients will be followed but will not receive adjuvant therapy. High risk patients will be randomized to: (1) CMF x 6 cycles; (2) CAF x 6 cycles; (3) CMF x 6 cycles followed by tamoxifen; or (4) CAF x 6 cycles followed by tamoxifen. Patients will start adjuvant chemotherapy within 12 weeks of definitive surgery. Patients who have had a breast sparing procedure and axillary dissection will receive radiation therapy, either before or after CMF or CAF (at the discretion of the treating physician). Radiotherapy and tamoxifen may be given together. Patients will be removed from the study for unacceptable toxicity, development of local/regional or metastatic disease; or noncancer related illnesses that prevent continuation of therapy or regular follow-up. Patients will be followed until death.

**Progress:** This study was closed to patient entry 1 Feb 93. Nine patients were enrolled in previous years and are still being followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 89/021	<b>Status:</b> On-going
<b>Title:</b> SWOG 8899: A Prospectively Randomized Trial of Low-Dose Leucovorin = 5-FU, High-Dose Leucovorin + 5-FU, Levamisole + 5-FU, or Low-Dose Leucovorin + 5-FU + Levamisole Following Curative Resection in...		
<b>Start Date:</b> 02/17/89	<b>Est. Completion Date:</b> Feb 92	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Howard Davidson, MC		
<b>Associate Investigators:</b>		COL Irwin B. Dabe, MC
MAJ Mark H. Kozakowski, MC		CPT Denis Bouvier, MC
MAJ Kenneth A. Bertram, MC		MAJ Everardo E. Cobos Jr., MC
<b>Key Words:</b> cancer:colon,resection,chemotherapy,leucovorin,levamisole		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$50.00	12/17/93

**Study Objective:** To assess the effectiveness of 5-FU + high-dose Leucovorin as surgical adjuvant therapy for resectable colon cancer, when compared to surgery alone.

**Technical Approach:** Patients must have received a potentially curative surgery for colon cancer with neither gross nor microscopic evidence of residual disease following the complete resection. The resected specimen must pathologically verify a diagnosis of modified Duke's B-2, B-3, or C. The primary tumor must be above the peritoneal reflection. Patients may not have had any prior chemotherapy nor exposure to 5-FU. Patients must be maintaining oral nutrition and be ambulatory 50% of the day and have adequate bone marrow function. Patients may not have a concurrent second malignant disease nor any previous malignant tumor within three years. Patients will be stratified by extent of invasion (limited to bowel wall vs into or through serosa vs perforation vs adherence to adjacent organs vs invasion of adjacent organs); extent of regional nodal metastases (none vs 0-4 vs >4); regional/ mesenteric implants resected enbloc (yes/no); and obstruction (yes/no). RANDOMIZE TO: (1) Observation; (2) Leucovorin 20 mg/m<sup>2</sup> + 5-FU 425 mg/m<sup>2</sup>; days 1-5; repeat at 4 and 8 wks, then every 5 wks for a total of 6 courses; (3) Leucovorin 500 mg/m<sup>2</sup> + 5-FU 600 mg/m<sup>2</sup>; Leucovorin by IV 2 hour infusion, 5-FU IV push beginning 1 hr after start of Leucovorin infusion, repeated weekly for 6 wks, followed by a 2-wk rest period, each 8-wk cycle (1 course) will be repeated for 4 courses. Revision (Jan 90): Observation arm closed (due to positive results seen in SWOG 8591); two new arms added (5-FU + levamisole & 5-FU + low dose leucovorin + levamisole).

**Progress:** Eighteen patients were enrolled at MAMC prior to closure to patient entry on 30 Jul 92. One patient was lost to follow-up, five patients have died from their disease and 12 continue to be followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 92/079		<b>Status:</b> On-going	
<b>Title:</b> SWOG 8925: Evaluation of Cisplatin + VP-16 Followed by Mitotane at Progression if no Prior Mitotane or Cisplatin + VP-16 Only if Prior Treatment with Mitotane in Patients with Advanced and .....					
<b>Start Date:</b> 06/05/92			<b>Est. Completion Date:</b> Jul 97		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC					
<b>Associate Investigators:</b>					
LTC Luke M. Stapleton, MC		MAJ Paul C. Sowray, MC			
MAJ Patrick L. Gomez, MC		MAJ Kenneth A. Bertram, MC			
MAJ Robert L. Sheffler, MC		MAJ Robert B. Ellis, MC			
MAJ Richard C. Tenglin, MC		CPT Jennifer L. Cadiz, MC			
		CPT James S. D. Hu, MC			
<b>Key Words:</b> cancer, adrenal, cisplatin, mitotane, VP-16					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		12/17/93	

**Study Objective:** To evaluate response and response duration of patients with adrenocortical carcinoma treated with combination chemotherapy consisting of cisplatin and etoposide and of patients who receive mitotane after progression on the above chemotherapy (if no prior treatment with mitotane); to evaluate the qualitative and quantitative toxicities of these therapies; and to evaluate and compare tumor morphology of patients with rare tumor.

**Technical Approach:** Patients will be placed in one of two treatment groups. Patients in Group A will not have received any prior chemotherapy. Patients in Group B will have received prior treatment with Mitotane. Eligible patients in Group A and Group B will be treated with cisplatin plus etoposide every 21 days for a total of 12 months or until progression of disease occurs. Group A patients who develop progressive disease will be treated with Mitotane. Group B patients who progress will be taken off protocol.

**Progress:** No patients have been enrolled in this study at MAMC

### Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 91/089

**Status:** On-going

**Title:** SWOG 8947: Central Lymphoma Serum Repository Protocol; Companion Protocol to SWOG Studies 8516, 8736, 8809, and 8816

**Start Date:** 08/02/91

**Est. Completion Date:**

**Department:** SWOG

**Facility:** MAMC

**Principal Investigator:** LTC Luke M. Stapleton, MC

**Associate Investigators:**

MAJ Paul C. Sowray, MC

MAJ Everardo E. Cobos Jr., MC

MAJ Robert B. Ellis, MC

CPT Jennifer L. Cadiz, MC

MAJ Kenneth A. Bertram, MC

LTC Howard Davidson, MC

MAJ Patrick L. Gomez, MC

MAJ Robert L. Sheffler, MC

MAJ Richard C. Tenglin, MC

CPT James S. D. Hu, MC

**Key Words:** lymphoma:serum repository

**Accumulative**

**Est. Accumulative**

**Periodic Review:**

**MEDCASE Cost:** \$0.00

**OMA Cost:** \$0.00

12/17/93

**Study Objective:** To establish a central lymphoma serum repository that will serve as a resource to provide specimens for current and future scientific studies and to utilize the Southwest Oncology Group clinical data base to perform clinicopathologic correlations with the results of those studies.

**Technical Approach:** No therapy will be utilized in this study and patient treatment will not be based on this study. Patients must meet the eligibility criteria and be registered to one of the following SWOG protocols: 8516, 8809, 8736, or 8816. Ten cc's of blood will be drawn prior to protocol treatment and shipped to the SWOG Lymphoma Serum Repository at Loyola University Medical School.

**Progress:** This is a companion protocol to other SWOG studies. Two specimens have been collected in previous years (0 in FY95).

### Detail Summary Sheet

**Date:** 30 Sep 95      **Protocol No.:** 91/006      **Status:** On-going

**Title:** SWOG 8952 (INT-0111), (CALG-8952), EST-5487): Treatment of Advanced Hodgkin's Disease - A Randomized Phase III Study Comparing ABVD vs MOPP/ABV Hybrid

**Start Date:** 10/19/90      **Est. Completion Date:**

**Department:** SWOG      **Facility:** MAMC

**Principal Investigator:** MAJ William A. Phillips

<b>Associate Investigators:</b>	LTC Howard Davidson, MC
MAJ Paul C. Sowray, MC	MAJ Patrick L. Gomez, MC
LTC Luke M. Stapleton, MC	MAJ Everardo E. Cobos Jr., MC
MAJ Robert L. Sheffler, MC	MAJ Robert B. Ellis, MC
CPT Jennifer L. Cadiz, MC	

**Key Words:** Hodgkin's disease, ABVD, MOPP, ABV Hybrid

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	12/17/93

**Study Objective:** To compare ABVD to the MOPP/ABV hybrid as therapy for patients with advanced Hodgkin's disease in terms of complete response rates, disease-free survival, failure-free survival, and both immediate and long term toxicities; to compare the rate of drug delivery of the anti-neoplastic agents, especially the comparative dose rate of ABV in the two treatment groups; and to examine the prognostic importance of time to response, performance status, age, presence of bulky disease, C-reactive protein, erythrocyte sedimentation rate, and prior radiotherapy on survival.

**Technical Approach:** Until recently, MOPP (nitrogen mustard, vincristine, procarbazine, prednisone) was the standard therapy for advanced Hodgkin's disease. In recent studies, the efficacy of AVBD (doxorubicin, bleomycin, vinblastine, DTIC) containing regimens has been equivalent to or superior to MOPP alone. Eligible patients will be those with histologically documented Hodgkin's disease so advanced that chemotherapy is the treatment of choice. Patients will be randomized to ABVD (all drugs given IV, days 1 and 15) or the MOPP/ABV hybrid (nitrogen mustard and vincristine IV day 1, oral procarbazine days 1-7, oral prednisone days 1-14, and doxorubicin, bleomycin, and vinblastine IV day 8. Cycles will be repeated every 28 days for 6 cycles unless disease progression is documented. At the end of 6 cycles, patients identified to be in complete response will receive an additional two cycles. Patients in partial response will be treated until they reach a complete response and then receive two further cycles for a maximum of 10 cycles.

**Progress:** No patients have been entered in this study at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 91/007		<b>Status:</b> On-going	
<b>Title:</b> SWOG 8957: Feasibility Trial of Post-Operative Radiotherapy Plus Cisplatin Followed by Three Courses of 5-FU Plus Cisplatin in Patients with Resected Head and Neck Cancer, Phase II Pilot					
<b>Start Date:</b> 10/19/90			<b>Est. Completion Date:</b>		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Patrick L. Gomez, MC					
<b>Associate Investigators:</b> MAJ Paul C. Sowray, MC LTC Luke M. Stapleton, MC MAJ Robert L. Sheffler, MC CPT Jennifer L. Cadiz, MC			LTC Howard Davidson, MC MAJ William A. Phillips MAJ Everardo E. Cobos Jr., MC MAJ Robert B. Ellis, MC		
<b>Key Words:</b> cancer:head & neck,radiotherapy,cisplatin,5-Fluorouracil					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$9130.00		12/17/93	

**Study Objective:** To evaluate the feasibility of administering three courses of chemotherapy to resected patients who have received cisplatin and radiation therapy post-operatively and to evaluate the qualitative and quantitative toxicities.

**Technical Approach:** Patients who have had resected squamous cell carcinoma of the oral cavity, oropharynx, hypopharynx, or larynx are eligible for the study. Chemotherapy used prior to surgery or radiotherapy in untreated head and neck cancer patients has produced particularly high rates of response. However, previous studies have shown that 20-25% of these patients will refuse further surgery or radiotherapy because of an initial good overall response with chemotherapy alone. To avoid this problem, the chemotherapy in this study will be given after surgery, along with radiation and as maintenance afterwards. Cisplatin, 100 mg/m<sup>2</sup>, on days 1, 22, and 43 will be given concomitant with radiation therapy. Three to four weeks post-radiation therapy, maintenance chemotherapy will be started. Maintenance chemotherapy will consist of cisplatin, 100 mg/m<sup>2</sup>, day 1 every 21 days for three courses and 5-FU, 1000 mg/m<sup>2</sup>, days 1-4, every 21 days for three courses.

**Progress:** One patient was enrolled in FY92 and is still being followed. This study closed to patient entry 1 May 92.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 91/021	<b>Status:</b> On-going
<b>Title:</b> SWOG 8990: (ECOG-9228, INT-0103): Combined Modality Treatment for Resectable Metastatic Colorectal Carcinoma to the Liver; Surgical Resection of Hepatic Metastases in Combination with Continuous .....		
<b>Start Date:</b> 12/07/90	<b>Est. Completion Date:</b>	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ William A. Phillips		
<b>Associate Investigators:</b>		
MAJ Paul C. Sowray, MC	LTC Howard Davidson, MC	
MAJ Everardo E. Cobos Jr., MC	LTC Luke M. Stapleton, MC	
MAJ Robert L. Sheffler, MC	MAJ Patrick L. Gomez, MC	
CPT Jennifer L. Cadiz, MC	MAJ Robert B. Ellis, MC	
	COL Joseph F. Homann, MC	
<b>Key Words:</b> cancer:colorectal,resection,chemotherapy,liver		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	12/17/93

**Study Objective:** To study the effects of long-term continuous infusion of Floxuridine (FUDR) intra-arterially and 5-FU systemically as therapy for liver metastases from colorectal primaries and to study the incidence of recurrence and time to recurrence in patients with 1-3 hepatic metastases treated with resection and continuous infusion of 5-FU into the systemic venous system and FUDR into the hepatic artery.

**Technical Approach:** This study attempts to combine surgical resection with long term hepatic artery infusion of chemotherapy and continuous infusion 5-FU. Patients with histologic confirmation of colorectal primary carcinoma and evidence of 1-3 liver metastases wither on CAT scan, liver scan or previous laparotomy, with no metastatic disease other than to the liver will be randomized to either surgery plus observation or sugary plus FUDR and 5-FU. FUDR will be given 0.1 mg/kg/day continuously for 14 days via Infusaid pump or arterial subcutaneous device. This cycle will be repeated every 28 days for 4 cycles. 5-FU will be given 200 mg/m<sup>2</sup>/day IV continuously for 14 days via permanent IV access device beginning of day 15 of each 28 day cycle and repeated for 4 cycles. When FUDR therapy ends, the IV dosage of 5-FU will be escalated to 300 mg/m<sup>2</sup>/day IV continuously for 14 days and repeated every 28 days for eight more cycles.

**Progress:** No patients have entered this study at MAMC.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/131		<b>Status:</b> On-going
<b>Title:</b> SWOG 8994: Evaluation of Quality of Life in Patients with Stage C Adenocarcinoma of the Prostate Enrolled on SWOG 8794				
<b>Start Date:</b> 08/05/94		<b>Est. Completion Date:</b> Jun 01		
<b>Department:</b> SWOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ J. Brantley Thrasher, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> Cancer:prostate, surgery, radiation therapy				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	//

**Study Objective:** To compare these primary aspects of quality of life, according to treatment assignment: 1) Treatment specific symptoms 2) Physical Functioning 3) Emotional functioning To compare three secondary quality of life variables, according to treatment assignment: 1) General symptoms 2) Global perception of quality of life 3) Social functioning

**Technical Approach:** This is a companion to SWOG 8794. Patients will be assigned to the same treatment groups as in the companion protocol (prostatectomy followed by adjuvant radiotherapy versus prostatectomy alone) and must be able to complete a quality of life questionnaire prior to registration and randomization on SWOG-8794. Standardized instructions will be read to the patients by the nurse/data manager at each site. Additional questionnaires will be completed at week 6, 6 months, 12 months, and then yearly for the next 4 years. Quality of life profiles will be compared for the two treatment groups at different points in time: baseline, where no differences are expected six weeks, where the two treatment groups are expected to show maximum differences on some measures; six months, one year and annually for a total for five years, where the treatment means for quality of life measures are expected to come together and level off. For key continuous variables, repeated measures analyses of variance should help to make comparisons at fixed points in time and across time. For the discrete variables such as occurrence or non-occurrence of specified complications, standard methods of categorical data analysis will be employed.

**Progress:** One patient was enrolled in FY95 and continues to be followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 90/056	<b>Status:</b> On-going
<b>Title:</b> SWOG 8997 (ECOG 3887): Phase III Chemotherapy of Disseminated Advanced Stage Testicular Cancer with Cisplatin Plus Etoposide with Either Bleomycin or Ifosfamide		
<b>Start Date:</b> 03/16/90	<b>Est. Completion Date:</b> Mar 93	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Howard Davidson, MC		
<b>Associate Investigators:</b>		
MAJ Mark H. Kozakowski, MC	MAJ Paul C. Sowray, MC	
MAJ Patrick L. Gomez, MC	MAJ Everardo E. Cobos Jr., MC	
MAJ Kenneth A. Bertram, MC	CPT Denis Bouvier, MC	
LTC John A. Vaccaro, MC	MAJ Robert L. Sheffler, MC	
<b>Key Words:</b> cancer:testicular,chemotherapy,cisplatin,bleomycin,ifosfamide		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$12862.00	<b>Periodic Review:</b> 12/17/93

**Study Objective:** To determine the objective response rate and duration of remission of BEP compared to VIP combination chemotherapy; to determine the toxicity of VIP compared to BEP combination chemotherapy; to confirm the efficacy and toxicity of intravenous Mesna as a urothelial protective agent.

**Technical Approach:** Patients must have a histologic diagnosis of advanced disseminated germ cell tumor and no prior chemotherapy or radiation therapy. Patients will be randomized to VIP (cisplatin, ifosfamide, mesna, and etoposide) to BEP (cisplatin, etoposide, and bleomycin). The regimen will be repeated every three weeks for four cycles. Bleomycin will be omitted for postsurgery chemotherapy in BEP patients. Patients in complete remission at the end of four courses of therapy will receive no further treatment. If there is radiographic or serologic evidence of persistent disease and residual tumor is surgically resectable, surgery will be performed. Patients who have complete or near complete resection of residual radiographic abnormalities with the pathologic finding of fibrosis/necrosis and those who have complete resection of mature or immature teratoma will receive no further treatment. Patients who have complete resection of residual disease which histologically shows viable carcinoma will receive two more courses of the original induction therapy. If residual tumor is deemed unresectable, patients will be followed monthly until disease progression with no further therapy. If relapse occurs in complete or partial responders less than 4 weeks after day 1 of the last course of induction therapy, the patient will be taken off study.

**Progress:** Prior to closure to patient entry (9 Apr 92) two patients had been enrolled at MAMC. One patient is still being followed (one died Jan 93).

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 93/056	<b>Status:</b> On-going
<b>Title:</b> SWOG 9003: Fludarabine for Waldenstrom's Macroglobulinemia (WM): A Phase II Study for Untreated and Previously Treated Patients		
<b>Start Date:</b> 03/05/93	<b>Est. Completion Date:</b> Mar 98	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Howard Davidson, MC		
<b>Associate Investigators:</b>		
MAJ Kenneth A. Bertram, MC	LTC Luke M. Stapleton, MC	
MAJ Timothy P. Rearden, MC	MAJ Patrick L. Gomez, MC	
MAJ Robert B. Ellis, MC	MAJ Mark E. Robson, MC	
MAJ Richard C. Tenglin, MC	CPT Jennifer L. Cadiz, MC	
LTC Robert D. Vallion, MC	CPT James S. D. Hu, MC	
	CPT Diana S. Willadsen, MC	
<b>Key Words:</b> Waldenstrom's Macroglobulinemia		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$3352.00	12/17/93

**Study Objective:** 1) To estimate response rates and survival in patients with Waldenstrom's Macroglobulinemia (WM) receiving fludarabine, with stratification according to whether they have prior therapy. 2) To define prognostic factors that may relate to response, time to progression and overall survival, separately for newly diagnosed and previously treated patients. 3) To estimate the associated hematologic and non-hematologic toxicities.

**Technical Approach:** Persons with a diagnosis of WM and meeting enrollment criteria can be registered for this study. After the initial workup, to include bone marrow aspiration, those patients without symptoms and with no progression of the disease will be entered in the Observation phase. If they are symptomatic or have progression of the disease or if onset of symptoms and/or progression occurs during the Observation phase immediate Re-registration to the Treatment phase will occur. Fludarabine 30 mg/m<sup>2</sup> IV will be administered on days 1 - 5. This schedule will be repeated every 28 days for 4 cycles until the patient's condition is stable without remission, progression occurs, or the disease is stable. If the disease becomes stable without remission or progresses, treatment will be stopped. If there is complete remission, partial remission or improvement the patient will receive an additional 4 cycles of therapy or 2 cycles beyond maximum response, whichever occurs earlier.

**Progress:** Two patients were enrolled in FY 93 and are still being followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 91/094		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9007: Cytogenetic Studies in Leukemia Patients, Ancillary					
<b>Start Date:</b> 09/06/91			<b>Est. Completion Date:</b>		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Kenneth A. Bertram, MC					
<b>Associate Investigators:</b>			LTC Howard Davidson, MC		
MAJ Paul C. Sowray, MC			LTC Luke M. Stapleton, MC		
MAJ Patrick L. Gomez, MC			MAJ Robert L. Sheffler, MC		
MAJ Robert B. Ellis, MC			MAJ Richard C. Tenglin, MC		
CPT Jennifer L. Cadiz, MC			CPT James S. D. Hu, MC		
<b>Key Words:</b> cancer:leukemia,cytogenetic studies					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>OMA Cost:</b>			
\$0.00		\$0.00		12/17/93	

**Study Objective:** To estimate the frequencies and prognostic significance of cytogenetic abnormalities in marrow or blood cells of leukemia patients prior to treatment on SWOG protocols and at various times in the course of treatment; to estimate correlations between the presence of cytogenetic features and of clinical, pathophysiological, cellular, or molecular characteristics in these patients; and to provide quality control for all SWOG cytogenetic data.

**Technical Approach:** The complex nature and diversity of numerical and structural chromosomal changes in hematologic malignancies have been increasingly recognized in the last 15 years as cytogenetic techniques have improved and the knowledge base expanded. It has been shown that the majority of malignancies have non-random chromosomal anomalies such that specific cytogenetic aberrations are generally associated with particular leukemia subtypes. Previous studies have shown the remarkable consistency of the recurring chromosome abnormalities in the leukemias and their current and potential usefulness as diagnostic and prognostic indicators. Strong correlations with certain clinical immunological and morphologic features have been shown and in certain cases a molecular mechanism has been discovered. Large prospective studies which include responsiveness to the various treatments have not been done and for most leukemias the molecular mechanisms and correlations remain to be elucidated. Patients on this study must be registered on one of the following SWOG protocols: 8326, 8600, 8612, 9034, 9108, and all new leukemia protocols approved as of 1990 by SWOG. Patients will receive treatment as directed by the treatment protocols and the treatment protocols will specify when specimens are to be submitted for cytogenetic analysis. Bone marrow samples will be submitted whenever possible, unless the treatment protocol specifies otherwise. However, if the marrow is not aspirable ("dry tap"), a peripheral blood sample will be submitted. A patient may only be registered on this protocol once. Data will be collected by major categories of leukemia: first line AML, first line ALL, relapsed AML, chronic phase CML, CML patients in acceleration or blast crisis; and hairy cell leukemia. The study will be open for accrual of patients for a minimum of five years. The smallest group of patients (CML in acceleration or blast crisis) is expected to have at least 100 patients by that time.

**Progress:** Five patients were entered in this study at MAMC in previous years. Three are deceased and two are being followed.

### Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 92/051

**Status:** On-going

**Title:** SWOG 9008: Trial of Adjuvant Chemoradiation After Gastric Resection for Adenocarcinoma, Phase II

**Start Date:** 04/03/92

**Est. Completion Date:** Mar 95

**Department:** SWOG

**Facility:** MAMC

**Principal Investigator:** LTC Luke M. Stapleton, MC

**Associate Investigators:**

MAJ Rahul N. Dewan, MC

MAJ Patrick L. Gomez, MC

MAJ Robert L. Sheffler, MC

MAJ Richard C. Tenglin, MC

LTC Howard Davidson, MC

MAJ Kenneth A. Bertram, MC

MAJ Robert B. Ellis, MC

CPT Jennifer L. Cadiz, MC

CPT James S. D. Hu, MC

**Key Words:** cancer, gastric, adenocarcinoma, chemoradiation

**Accumulative**

**MEDCASE Cost:** \$0.00

**Est. Accumulative**

**OMA Cost:** \$0.00

**Periodic Review:**

12/17/93

**Study Objective:** To evaluate the possible benefit of adjuvant chemoradiation therapy in patients with resected gastric cancer to include: comparison of overall and disease free survival between patients being treated with surgical resection only and those being treated with surgery plus adjuvant therapy; comparison of incidence and patterns of disease failure between surgery and surgery plus adjuvant therapy treated patients; and assessment of patient tolerance of upper abdominal chemoradiation after gastric resection.

**Technical Approach:** Patients will be randomized to either observation or adjuvant therapy. Adjuvant therapy will consist of one course of 5-FU and Leucovorin given IV. Four weeks later the patient will receive a second course of 5-FU with Leucovorin with concomitant radiation therapy. While receiving radiation therapy, the patient will receive a third course of 5-FU and Leucovorin, which will occur during the fifth week of radiation therapy. After completing radiation therapy, the patient will receive two additional courses of chemotherapy to begin approximately 35 days after completion of radiotherapy.

**Progress:** One patient was enrolled (FY 94) and continues to be followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 91/033		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9013 (RTOG 89-11, INT-0113): A Prospective Randomized Comparison of Combined Modality Therapy for Squamous Carcinoma of the Esophagus: Chemotherapy Plus Surgery Versus Surgery Alone for ....					
<b>Start Date:</b> 02/01/91			<b>Est. Completion Date:</b>		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Paul C. Sowray, MC					
<b>Associate Investigators:</b>			LTC Howard Davidson, MC		
MAJ William A. Phillips			LTC Luke M. Stapleton, MC		
MAJ Patrick L. Gomez, MC			MAJ Robert L. Sheffler, MC		
MAJ Robert B. Ellis, MC			CPT Jennifer L. Cadiz, MC		
COL Joseph F. Homann, MC			COL Daniel G. Cavanaugh, MC		
MAJ Everardo E. Cobos Jr., MC					
<b>Key Words:</b> cancer:esophagus,chemotheray,surgery,modality therapy					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	12/17/93	

**Study Objective:** To compare, using a prospective controlled randomized study design, the outcomes of therapy of surgery alone versus pre and postoperative chemotherapy and surgery for patients with local regional esophageal cancer (outcome is defined as survival and relapse pattern); to assess the toxicities of a multimodality approach to esophageal carcinoma involving systemic chemotherapy and surgery (the toxicities of surgical resection as initial therapy or following chemotherapy will be assessed as operative morbidity and mortality); to compare the local and distant control rates with the two approaches and to define the pattern of failure; and to compare the impact on overall and disease free survival of multimodality therapy with surgery alone.

**Technical Approach:** Esophageal cancer is seen in over 10,000 patients a year in the United States and only about 7% of these patients are cured as demonstrated by a five year survival. This study is designed to see whether or not giving chemotherapy will improve that survival. To be eligible patients must have histologic proof of squamous cell carcinoma of the esophagus, disease limited to the total regional area (clinical stage T1-T3, NX,MO), no prior surgery, radiation therapy, or chemotherapy, and adequate bone marrow, liver function, renal function, and pulmonary reserve. Patients must be physiologically fit for proposed chemotherapy and surgery and be greater than 18 years of age. Patients will be randomized to surgery alone, or to receive three cycles of preoperative cisplatin and 5-FU and then to undergo definitive surgery followed by two more cycles of cisplatin and 5-FU, starting two to six weeks after surgery.

**Progress:** Three patients have entered this study in previous years (1 in FY95). Two are being followed and one died of the disease.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/143		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9019: A Phase III, Randomized, Prospective Comparison Between Chemotherapy Plus Radiotherapy, and the Same Chemotherapy Plus Radiotherapy Together With Surgery for .... Non-Small Cell Lung Cancer					
<b>Start Date:</b> 06/09/93			<b>Est. Completion Date:</b> May 98		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Patrick L. Gomez, MC					
<b>Associate Investigators:</b>					
LTC Luke M. Stapleton, MC			LTC Howard Davidson, MC		
MAJ Timothy P. Rearden, MC			MAJ Kenneth A. Bertram, MC		
MAJ Robert B. Ellis, MC			MAJ Mark E. Robson, MC		
MAJ Richard C. Tenglin, MC			CPT Jennifer L. Cadiz, MC		
LTC Robert D. Vallion, MC			CPT James S. D. Hu, MC		
			CPT Diana S. Willadsen, MC		
<b>Key Words:</b> cancer:non-small cell lung					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		12/17/93	

**Study Objective:** (1) To assess whether concurrent chemotherapy and radiotherapy, followed by surgical resection, results in a significant improvement in progression-free, overall, and long-term survival compared to the same chemotherapy plus standard radiotherapy alone for patients with stage IIIa (N2 Positive) and selected IIIB non-small cell lung cancer. (2) To evaluate the patterns of local and distant failure for patients enrolled in each arm of the study, in order to assess the impact of the therapy on local control and distant metastasis.

**Technical Approach:** Patients with regionally advanced non-small cell lung carcinoma will be randomized to one of two arms. Arm I: patients will receive induction radiation therapy to a "tight" field to 4500 cGy. They will receive concurrent cisplatin on days 1 and 8 and on days 29 & 36 with VP-16 days 1-5, repeated on days 29-33 (2 cycles). After completion of induction, patients will be re-evaluated for extent of disease. If there is no progression of the disease, patients will go to exploratory thoracotomy for complete removal of the primary lesion and sampling of nodes.

If the tumor is unresectable or the margins are positive or the mediastinal nodes are positive, an additional 2 cycles of chemotherapy with a radiation boost will be given. Patients who complete the induction phase but have persistent supraclavicular node metastases will also receive 2 more cycles of concurrent chemo-radiotherapy will not go to surgery.

Arm II patients receive "standard" lung field radiation therapy to 4500 cGy and concurrent cisplatin and VP-16 for 2 cycles.

One week prior to completing radiation therapy, patients will be re-evaluated for response. Those patients with no evidence of distant metastases or local progression will continue radiation therapy with no break for an additional 1600 cGy with a boost. They will also receive 2 more cycles of chemotherapy concurrent with radiation.

Any patient who shows local or distant progression after induction chemo-radiation will be taken off protocol..

**Progress:** Two patients have been enrolled in this study in previous years (1 in FY95). One patient continues to be followed and the other died of the disease.

## Detail Summary Sheet

**Date:** 30 Sep 95      **Protocol No.:** 92/052      **Status:** On-going

**Title:** SWOG 9031: A Double Blind Placebo Controlled Trial of Daunomycin and Cytosine Arabinoside With or Without rhG-CSF in Elderly Patients With Acute Myeloid Leukemia, Phase III

**Start Date:** 04/03/92      **Est. Completion Date:** Jun 94

**Department:** SWOG      **Facility:** MAMC

**Principal Investigator:** MAJ Kenneth A. Bertram, MC

<b>Associate Investigators:</b>	LTC Howard Davidson, MC
MAJ Paul C. Sowray, MC	LTC Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC	MAJ Robert B. Ellis, MC
MAJ Robert L. Sheffler, MC	CPT Jennifer L. Cadiz, MC
MAJ Richard C. Tenglin, MC	CPT James S. D. Hu, MC

**Key Words:** cancer, leukemia, myeloid

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	12/17/93

**Study Objective:** To compare the complete response rates and duration of survival in patients 56 or older with acute myeloid leukemia (AML) when treated with standard doses of cytosine arabinoside (Ara-C) and daunorubicin (DNR), with or without recombinant human granulocyte-colony stimulating factor (rhG-CSF); to assess the frequency and severity of toxicities of the two treatment regimens; to compare the duration of neutropenia and thrombocytopenia, the total number of febrile days, the number of days of antibiotic therapy, the number and type of infection episodes, and the number of hospital days in patients treated with or without rhG-CSF; and to correlate biological parameters including cell surface immunophenotype, ploidy, and cytogenetics with clinical response.

**Technical Approach:** Patients aged 56 and older with AML will be randomized to receive treatment with either Ara-C/DNR plus rhG-CSF or Ara-C/DNR plus placebo (Ara-C days 1-7, C/DNR days 1-3, and blinded drug begins on day 10) Patients who had regrowth of leukemia during this course of treatment will receive a second identical course of treatment except the blinded drug will not be started until the marrow shows <5% blasts. The blinded drug will not be given in the second induction course if the patient has regrowth of leukemia following the first induction course. Following completion of induction therapy, patients who achieve complete remission will be registered to receive two cycles of post-remission therapy, utilizing the same regimen to which they were originally randomized.

**Progress:** Two patients have been enrolled in this study in in previous years. One is deceased and one is being followed. This study closed to patient accrual 1 Jan 95.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 92/095		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9032: A Controlled Trial of Cyclosporine as a Chemotherapy-Resistance Modifier in Blast Phase Chronic Myelogenous Leukemia					
<b>Start Date:</b> 08/07/92			<b>Est. Completion Date:</b> Sep 94		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Kenneth A. Bertram, MC					
<b>Associate Investigators:</b>			LTC Howard Davidson, MC		
LTC Luke M. Stapleton, MC			MAJ Patrick L. Gomez, MC		
MAJ Robert B. Ellis, MC			CPT Jennifer L. Cadiz, MC		
MAJ Richard C. Tenglin, MC			CPT James S. D. Hu, MC		
<b>Key Words:</b> cancer, myelogenous, leukemia					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		12/17/93	

**Study Objective:** To compare the duration of survival in patients with chronic myelogenous leukemia (CML) in blast phase, when treated with either chemotherapy (Ara-C/Daunomycin) alone or chemotherapy plus the resistance modifier, cyclosporine-A (CyA); to estimate the frequency of P-glycoprotein expression and its association with blast lineage and prognosis; and to compare the frequency and severity of toxicity of the two treatment regimens.

**Technical Approach:** Patients will be randomized to receive treatment with either Ara-C/Daunomycin alone or Ara-C/Daunomycin + CyA. If the day 14 bone marrow shows less than or equal to a 50% reduction in the absolute blast count per 500 cell differential compared with the pretreatment bone marrow, the patient will be considered a treatment failure and removed from the study. If there is more than a 50% reduction in the blast count as stated above, but the patient has not achieved a complete remission or restored chronic phase status, a second course of the original induction regimen will begin on or after day 21. Patients who do not achieve complete remission or restoration of chronic phase after two inductions will be removed from the protocol. Patients who achieve complete remission or restored chronic phase will receive one course of consolidation therapy (same regimen as for induction therapy).

**Progress:** No patients have been entered at MAMC. Patient accrual continues.

### Detail Summary Sheet

**Date:** 30 Sep 95      **Protocol No.:** 93/067      **Status:** Completed

**Title:** SWOG 9034 (EST 3489, CALGB 9120): Phase III Study of Three Intensive Postremission Therapies in Adult Acute Nonlymphocytic Leukemia: Comparison of Autologous Bone Marrow Transplantation, Intensive....

**Start Date:** 03/05/93

**Est. Completion Date:** Apr 95

**Department:** SWOG

**Facility:** MAMC

**Principal Investigator:** MAJ Mark E. Robson, MC

**Associate Investigators:**  
LTC Howard Davidson, MC  
MAJ Patrick L. Gomez, MC  
MAJ Robert B. Ellis, MC  
CPT James S. D. Hu, MC  
LTC Robert D. Vallion, MC

LTC Luke M. Stapleton, MC  
MAJ Kenneth A. Bertram, MC  
MAJ Timothy P. Rearden, MC  
CPT Jennifer L. Cadiz, MC  
MAJ Richard C. Tenglin, MC  
CPT Diana S. Willadsen, MC

**Key Words:** cancer:leukemia, autologous bone marrow, allogenic bone marrow, idarubicin, Ara-C, busulfan, cyclophosphamide

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	12/17/93

**Study Objective:** 1. To compare complete remission (CR) duration and survival in de novo acute myelogenous leukemia resulting from post-remission therapy with 4-HC treated marrow versus conventional chemotherapy versus one course of high-dose cytarabine. 2. To examine differences in outcome for allogeneic bone marrow transplantation versus consolidation therapy or autologous transplant. 3. To examine the results of differing post-remission therapies in patient subsets defined by age, cell surface markers, and karyotype abnormalities.

**Technical Approach:** Patients having morphologic proof of non-lymphocytic leukemia, who have not been previously treated with radiation therapy or cytologic chemotherapy, are eligible for this study. Following registration, induction with Idarubicin 12 mg/m<sup>2</sup>/day on days 1, 2, & 3 and Cytidine 25 mg/m<sup>2</sup> IV push, then 100 mg/m<sup>2</sup> by continuous infusion on days 1, 2, 3, 4, 5, 6, & 7. Patients will receive a second course of the induction medication (Ida/Ara-C) if a remission is not achieved from the first. Patients failing to receive a complete remission (CR) after the 2nd induction Ida/Ara-C course are off study. Patients achieving CR who have a histocompatible sibling will receive an Allogeneic Bone Marrow Transplantation (using Busulfan-Cyclophosphamide as the preparative regimen. Patients not qualified for allogeneic transplant will then be randomized to either an Autologous Bone Marrow Transplantation or Consolidation Chemotherapy with Cytarabine 3 gm/m<sup>2</sup> IV over 1 hour every 12 hours X 12 doses (6 days). The preparative therapy for the autologous transplant is Busulfan 1 mg/kg q6 hr X 16 (4 days) followed by Cyclophosphamide 50 mg/kg IV q.d. X 4.

**Progress:** One patient was enrolled in this study in FY93 and is now deceased. This study closed to patient accrual 1 Feb 95.

### Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 95/062

**Status:** On-going

**Title:** SWOG 9035: Randomized Trial of Adjuvant Immunotherapy with an Allogeneic Melanoma Vaccine for Patients with Intermediate Thickness, Node Negative Malignant Melanoma, Phase III

**Start Date:** 01/20/95

**Est. Completion Date:** Jan 99

**Department:** SWOG

**Facility:** MAMC

**Principal Investigator:** MAJ Richard F. Williams, MC

**Associate Investigators:**

LTC Howard Davidson, MC  
MAJ Timothy P. Rearden, MC  
CPT James S. D. Hu, MC  
CPT Diana S. Willadsen, MC

LTC Luke M. Stapleton, MC  
MAJ Kenneth A. Bertram, MC  
MAJ Robert B. Ellis, MC  
LTC Robert D. Vallion, MC  
CPT John R. Caton, MC

**Key Words:** Cancer:melanoma, immunotherapy, vaccine

**Accumulative**

**MEDCASE Cost:** \$0.00

**Est. Accumulative**

**OMA Cost:** \$0.00

**Periodic Review:**

//

**Study Objective:** 1) To compare disease-free survival and overall survival between patients with T3NOM0 malignant melanoma who receive adjuvant immunotherapy with an allogeneic melanoma vaccine versus no adjuvant treatment. 2) To evaluate the toxicity of adjuvant immunotherapy with an allogeneic melanoma vaccine in patients with T3NOI10 malignant melanoma. 3) To explore the interaction between the patients' defined HLA types (i.e., whether they are compatible with the HLA phenotypes of the vaccine) and the vaccine treatment effectiveness in terms of disease-free survival and overall survival.

**Approach:** The study is a randomized study of Interferon Alfa-2b as adjuvant immunotherapy in patients with T3NOM0 malignant melanoma following complete resection. After complete staging, including assessment of any abnormal lymph nodes by biopsy, patients will be randomized either to treatment with four cycles of intramuscular vaccine therapy or observation only and will be followed until death for recurrence

**Progress :** One patient has been enrolled in FY95 at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 91/077	<b>Status:</b> On-going
<b>Title:</b> SWOG 9039: Evaluation of Quality of Life in Patients with Stage D2 Cancer of the Prostate Enrolled on SWOG 8894		
<b>Start Date:</b> 07/12/91	<b>Est. Completion Date:</b>	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Paul C. Sowray, MC		
<b>Associate Investigators:</b>		
MAJ William A. Phillips	LTC Howard Davidson, MC	
MAJ Everardo E. Cobos Jr., MC	LTC Luke M. Stapleton, MC	
MAJ Robert L. Sheffler, MC	MAJ Patrick L. Gomez, MC	
CPT Jennifer L. Cadiz, MC	MAJ Robert B. Ellis, MC	
<b>Key Words:</b> cancer:prostate,quality of life		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	12/17/93

**Study Objective:** To compare three primary quality of life endpoints according to treatment assignment: (1) treatment specific symptoms, (2) physical functioning, (3) emotional functioning; and to compare four secondary quality of life variables, according to treatment assignment: (1) general symptoms, (2) role functioning, (3) global perception of quality of life, (4) social functioning.

**Technical Approach:** This cancer control intervention study measures quality of life in patients with advanced carcinoma of the prostate, specifically SWOG protocol 8894: Treatment of Stage D2 Carcinoma of the Prostate Comparing Orchiectomy +/- Flutamide. The presence or absence of flutamide provides the intervention for this cancer control companion study. Thus, the benefits of randomization, uniform patient selection, and treatment standardization are transferred to the quality of life investigation. The comparison of quality of life measurements between treatment arms will complement the analysis of survival and response data for patients registered to SWOG 8894 and become a critical consideration if no difference is demonstrated in survival between the treatment arms. The Quality of Life Questionnaire will be completed at study entry and at 1, 3, and 6 months after study entry.

**Progress:** One patient was enrolled in this protocol in FY93 and is still being followed. This study closed to patient entry 15 Sept 94.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 91/069	<b>Status:</b> On-going
<b>Title:</b> SWOG 9040 (CALGB-9081, INT-0014): Intergroup Sectal Adjuvant Protocol, A Phase III Study		

<b>Start Date:</b> 06/14/91	<b>Est. Completion Date:</b>
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<b>Department:</b> SWOG	<b>Facility:</b> MAMC
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**Principal Investigator:** LTC Howard Davidson, MC

<b>Associate Investigators:</b>	MAJ Everardo E. Cobos Jr., MC
MAJ Paul C. Sowray, MC	MAJ Patrick L. Gomez, MC
MAJ Rahul N. Dewan, MC	MAJ Steven S. Wilson, MC
MAJ Robert L. Sheffler, MC	MAJ Robert B. Ellis, MC
CPT Jennifer L. Cadiz, MC	

**Key Words:** cancer:rectum,5-Fluorouracil,leucovorin,levamisole

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	12/17/93

**Study Objective:** To determine the relative efficacy of: 5-FU; 5-FU plus leucovorin; 5-FU plus levamisole; and 5-FU plus leucovorin and levamisole when combined with pelvic radiation therapy in the treatment of Stages B-2 and C (TNM Stage II and III) rectal cancer. End points used will include local recurrence rates, probability of distant metastases, disease free survival rates, and overall survival.

**Technical Approach:** This will be a 4-armed study with the same radiation therapy program in all arms, but with varying drug regimens as listed in the objective. 5-FU with radiation therapy will comprise the control arm of the study. Patients will be randomized to treatment arms and they will be stratified by type of operation (abdominal perineal or anterior resection); nodal involvement (none, 1-3, or >3); and invasion through bowel wall or into adjacent organs (none, through muscularis propria, or adherence to or invasion of adjacent organs or structures). Each drug regimen will be given alone on days 1-5 and 29-33, followed by radiation therapy (five weeks) with concomitant chemotherapy on days 57-60 and 85-88. The chemotherapy regimen will then be repeated beginning 28 days after the completion of radiation therapy on days 1-5 and 29-33. If evidence of recurrence is obtained, protocol treatment will be discontinued and the patient followed until death. In the absence of recurrent disease, follow-up observations will be continued for a minimum of 5 years after surgery.

**Progress:** This study was closed to patient entry on 22 Nov 92. Three patients were enrolled in previous years and continue to be followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/104	<b>Status:</b> On-going
<b>Title:</b> SWOG 9041: Chemoprevention of Recurrent Adenomas and Second Primary Colorectal Carcinoma. A Phase III Pilot Study.		
<b>Start Date:</b> 05/06/94	<b>Est. Completion Date:</b> May 98	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Timothy P. Rearden, MC		
<b>Associate Investigators:</b>		
LTC Howard Davidson, MC	LTC Luke M. Stapleton, MC	
MAJ Patrick L. Gomez, MC	MAJ Kenneth A. Bertram, MC	
MAJ Robert B. Ellis, MC	MAJ Mark E. Robson, MC	
CPT James S. D. Hu, MC	MAJ Richard C. Tenglin, MC	
CPT Diana S. Willadsen, MC	LTC Robert D. Vallion, MC	
	MAJ Richard F. Williams, MC	
<b>Key Words:</b> Cancer: colorectal, chemoprevention, calcium carbonate		
<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	/ /

**Study Objective:** This is a preliminary effort towards the long-term research goal of determining whether calcium, as a nutritional supplement, can prevent colorectal adenomas and new primary carcinomas in surgically treated colorectal carcinoma (CRC) patients.

**Technical Approach:** Patients with previously resected colon cancer, Stages 0, I, or II or rectal carcinomas, Stages 0, I are eligible to participate in this study. During the 3 month Run In period, patients will be placed on placebo 3 tablet a day. After successful completion of the Run In (patients must have taken > 80% of tablets) patients will be randomized to regimen A (3 - 600 mg tablets of calcium carbonate daily for 5 years) or regimen b (3 placebo tablets daily for 5 years). The pills will be provided to the patients every three months for the first two years and every six months for the next three years. Patients will be monitored for compliance, hypercalcemia, renal toxicity and gastrointestinal or hepatic toxicity. Endpoint is the efficacy of supplemental oral calcium in reducing recurrence of adenomas or second primary carcinomas.

**Progress:** Seven patients have been entered in this study (6 in FY95), and all continue to be followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/032		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9061 (EST-2190, INT 0121): A Phase III Study of Conventional Adjuvant Chemotherapy vs High Dose Chemotherapy and Autologous Bone Marrow Transplantation....Breast Cancer at High Risk of Recurrence					
<b>Start Date:</b> 12/04/92			<b>Est. Completion Date:</b> Nov 95		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Timothy P. Rearden, MC					
<b>Associate Investigators:</b>			LTC Luke M. Stapleton, MC		
LTC Howard Davidson, MC			MAJ Kenneth A. Bertram, MC		
MAJ Patrick L. Gomez, MC			MAJ Mark E. Robson, MC		
MAJ Robert B. Ellis, MC			CPT Jennifer L. Cadiz, MC		
MAJ Richard C. Tenglin, MC			CPT James S. D. Hu, MC		
LTC Robert D. Vallion, MC			CPT Diana S. Willadsen, MC		
<b>Key Words:</b> cancer:breast, chemotherapy, bone marrow transplantation					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		12/17/93	

**Study Objective:** To compare the sites and rates of recurrence, disease-free survival and overall survival, and toxicity of adjuvant chemotherapy (CAF) with adjuvant chemotherapy plus high-dose therapy with cyclophosphamide and the TEPA with autologous marrow infusion in patients with breast cancer with 10 or more positive lymph nodes.

**Technical Approach:** Patients will be stratified according to estrogen receptor status, age, and menopausal status and then randomized to receive radiotherapy plus tamoxifen or high-dose chemotherapy and autologous bone marrow transplantation. Both arms will receive cyclophosphamide 100 mg/m<sup>2</sup> PO X 14 days, doxorubicin 30 mg/m<sup>2</sup> IV days 1 & 8, and flurouracil 500 mg/m<sup>2</sup> IV days 1 & 8 repeated every 28 days x 6 cycles (CAF). Patients receiving CAF without bone marrow transplantation will begin radiation therapy within 4 weeks of the last dose of chemotherapy or when the WBC > 2900 and Platelets > 100,000. Patients randomized to receive high-dose chemotherapy will have bone marrow harvested no sooner than 4 weeks nor longer than 8 weeks after the last previous dose of myelotoxic chemotherapy. The CBC must be normal and the bone marrow normocellular and free of tumor by bilateral iliac crest biopsy within 4 weeks prior to storage. After the bone marrow is harvested, high-dose chemotherapy of cyclophosphamide 6000 mg/m<sup>2</sup>/96 hr and ThioTEPA 800 mg/m<sup>2</sup>/96 hr (4 days), will be given by continuous infusion over 4 days, days -6 to -2. Autologous bone marrow reinfusion will be on day 0. Patients receiving BMT will again be randomized to receive GM-CSF as a daily 2, 6 or 24 hour intravenous infusion beginning 2-4 hours after bone marrow infusion. GM-CSF will be initiated at a dose of 250 mcg/m<sup>2</sup>/d. Treatment will continue until the patient has achieved an absolute neutrophil count (ANC) of ≥ 1000 cells/ul on 3 consecutive days or a planned duration of 28 days of treatment.

Tamoxifen 20 mg PO q.d. will be given to all patients who are estrogen or progesterone receptor positive after the completion of all chemotherapy for 5 years. For patients not randomized to receive transplant, Tamoxifen should be initiated 28 days after the start of the last CAF cycle. Patients randomized to receive transplant should begin Tamoxifen following transplant when WBC > 4000 and/or ANC > 2000. Patients will be taken off-study if there is development of metastatic disease at any time while

therapy is ongoing.

Measurement of effect is recurrence, disease-free survival or survival (survival is measured from the date of randomization to date of death).

At measured times during the study a Breast Chemotherapy Questionnaire (BCQ) will be completed to separately document the changes in psychosocial function that occur on the two regimens. Not all subjects will complete the questionnaire at all time points, but if at least 150 per arm have complete data, the width of a 95% confidence interval on the mean change in scores would be about  $\pm 0.09$ .

The BCG will also be used to make comparisons between regimens. A 2 degree of freedom test based on the difference of the means of the 36 week evaluation and the difference of the means of the 52 week evaluation will be used. Then using the variance information given above, the variance of the difference of means at either time should have a variance of about 0.0099, and the covariance between the two times should be about 0.0079. If there is a constant difference in the scores, then the distribution of the test statistic would be approximately noncentral chi-square with 2 degrees of freedom and centrality parameters  $113 \cdot d \cdot d$ . For a 5% level test, this gives a power of 82% for detecting a difference of  $d = 0.3$ .

Progress: No patients have entered this study at MAMC.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/144		<b>Status:</b> Completed	
<b>Title:</b> SWOG 9107: A Phase II Pilot Study of High-Dose 24-Hour Continuous Infusion 5-FU and Leucovorin and Low-Dose PALA for Patients With Colorectal Cancer					
<b>Start Date:</b> 06/09/93			<b>Est. Completion Date:</b> Jun 96		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Timothy P. Rearden, MC					
<b>Associate Investigators:</b>					
LTC Howard Davidson, MC			LTC Luke M. Stapleton, MC		
MAJ Patrick L. Gomez, MC			MAJ Kenneth A. Bertram, MC		
MAJ Robert B. Ellis, MC			MAJ Mark E. Robson, MC		
MAJ Richard C. Tenglin, MC			CPT Jennifer L. Cadiz, MC		
LTC Robert D. Vallion, MC			CPT James S. D. Hu, MC		
			CPT Diana S. Willadsen, MC		
<b>Key Words:</b> Cancer:colorectal, 5-FU, Leucovorin, PALA					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	12/17/95	

**Study Objective:** To evaluate response rates and toxicities of 5-FU 2600 mg/m<sup>2</sup> as a 24 hour continuous intravenous infusion given once a week, in combination with Leucovorin 500 mg/m<sup>2</sup> as a 24 hour continuous infusion and PALA 250 mg/m<sup>2</sup> intravenously.

**Technical Approach:** Patients with histologically proven diagnosis of colorectal cancer with distant metastasis who have received no more than one adjuvant chemotherapy will receive PALA IV on day 1 and Leucovorin and 5-FU 24 hours later. This regimen will be repeated on 7 day cycles and will continue until disease progression.

**Progress:** One patient entered this study at MAMC in FY93 and is now deceased. This study was closed to patient entry 1 Aug 94.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 91/096	<b>Status:</b> On-going
<b>Title:</b> SWOG 9108 (CALGB-9011, NCIC-CTG CL.1): A Phase III Comparison of Fludarabine Phosphate vs Chlorambucil vs Fludarabine Phosphate Plus Chlorambucil in Previously Untreated B-Cell Chronic Lymphocytic....		
<b>Start Date:</b> 09/06/91	<b>Est. Completion Date:</b>	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Kenneth A. Bertram, MC		
<b>Associate Investigators:</b>		
MAJ Paul C. Sowray, MC	LTC Howard Davidson, MC	
MAJ Patrick L. Gomez, MC	LTC Luke M. Stapleton, MC	
MAJ Robert B. Ellis, MC	MAJ Robert L. Sheffler, MC	
CPT Jennifer L. Cadiz, MC	MAJ Richard C. Tenglin, MC	
	CPT James S. D. Hu, MC	
<b>Key Words:</b> cancer:leukemia,B-cell,fludarabine phosphate,chlorambucil		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	12/17/93

**Study Objective:** To compare in previously untreated CLL patients the response rates and progression free survival with the following three therapeutic regimens: (1) fludarabine phosphate, (2) chlorambucil, and (3) fludarabine phosphate plus chlorambucil; to determine whether the quality of life (need for transfusions, incidence of infections, and performance status) is superior using any of the three regimens; and to determine whether these two drugs are non-cross-resistant by a crossover design for patients failing to respond to the single agent to which they were initially randomized.

**Technical Approach:** B-cell chronic lymphocytic leukemia (CLL) is the most common leukemia in adults. This study is designed to compare a new drug, fludarabine, (Arm I) to standard therapy, chlorambucil (an alkylating agent, Arm II), and to the combination of fludarabine and chlorambucil (Arm III). The drugs will be administered every four weeks until patients reach a complete remission or maximally beneficial response (up to one year of treatment). Patients with progressive disease on Arm I or II will crossover to the other single agent arm. After completing the prescribed treatment arm, patients may be re-entered if they relapse. Patients will be randomly assigned, with equal probabilities, to one of the three treatment arms. Randomization will be stratified by risk group and duration of disease with treatment allocations being adjusted as necessary and is still being followed

**Progress:** One patient was entered in this study in FY94 and continues to be followed. This study closed to patient entry 7 Dec 94.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/095		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9109: Neoadjuvant Zoladex and Flutamide in Bulky and Non-Bulky Clinical Stage C Carcinoma of the Prostate, Phase II					
<b>Start Date:</b> 04/01/94			<b>Est. Completion Date:</b> Apr 98		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ J. Brantley Thrasher, MC					
<b>Associate Investigators:</b>					
COL John C. Norbeck, MC		MAJ Kurt L. Hansberry, MC			
CPT Bradley F. Schwartz, MC		CPT Michael D. Bagg, MC			
LTC Howard Davidson, MC		LTC Luke M. Stapleton, MC			
MAJ Patrick L. Gomez, MC		MAJ Kenneth A. Bertram, MC			
		MAJ Timothy P. Rearden, MC			
<b>Key Words:</b> Cancer:prostate, Zoladex, Flutamide					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		/ /	

**Study Objective:** 1) To evaluate the resectability rate following 16 weeks of total androgen blockade therapy. 2) To evaluate the likelihood of clinical response to 16 weeks of total androgen blockade therapy. 3) To assess the feasibility of obtaining flow cytometry specimens for the purpose of evaluating the likelihood of an association between ploidy and clinical response or resectability. 4) To evaluate the qualitative and quantitative toxicities from total androgen blockade therapy and the immediate and long-term morbidity associated with radical prostatectomy and pelvic lymph node dissection following neoadjuvant total androgen blockade therapy. 5) To evaluate time to progression.

**Technical Approach:** Patients with Stage C, D0, and D1 prostate cancer will begin neoadjuvant total androgen blockade within 24 hours of registration. This treatment will consist of Zoladex 3.6 mg S.Q. every 4 weeks X 16 weeks and Flutamide 250 mg P.O. daily X 16 weeks. Patients will be evaluated by digital rectal exam at weeks 5, 9, 13 and 17, and trans-rectal ultrasound at weeks 9 and 17. After 16 weeks of androgen blockade, patients will be re-evaluated to undergo radical prostatectomy with pelvic lymph node dissection. Patients deemed operable will have surgery performed by week 17 or, if the treatment was interrupted, within one week of completing total androgen blockade. Following surgery, all patients, including those that were unresectable or partially resectable, will be followed for subjective/objective evidence of developing toxicities and progression of disease. Following surgery or attempted surgery, no additional therapy is to be given in the absence of progression, at which time patients will go off protocol treatment. Subsequent therapy off protocol treatment is at the discretion of the investigator.

**Progress:** No patients entered in this study at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 91/078	<b>Status:</b> Completed
<b>Title:</b> SWOG 9111: Post-Operative Adjuvant Interferon Alpha 2 in Resected High-Risk Primary and Regionally Metastatic Melanoma, Intergroup		
<b>Start Date:</b> 07/12/91	<b>Est. Completion Date:</b>	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Timothy P. Rearden, MC		
<b>Associate Investigators:</b>		
MAJ Everardo E. Cobos Jr., MC	LTC Howard Davidson, MC	
LTC Luke M. Stapleton, MC	MAJ Patrick L. Gomez, MC	
MAJ Robert L. Sheffler, MC	MAJ Kenneth A. Bertram, MC	
CPT Jennifer L. Cadiz, MC	MAJ Robert B. Ellis, MC	
	MAJ Paul C. Sowray, MC	
<b>Key Words:</b> melanoma,interferon alpha 2		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	12/17/93

**Study Objective:** To establish the efficacy of one year at maximally tolerable dosages (IV and SC) interferon alpha-2 as an adjuvant to increase the disease free interval and overall survival in patients at high risk for recurrence after definitive surgery for deep primary lesions or after regional lymph node recurrence; and to evaluate the efficacy and tolerance of long-term alpha-2 at 3 MU/d (Sc TIW) as an adjuvant in similar patients in comparison to 1 year of treatment of maximally tolerable dosages.

**Technical Approach:** Patients must fulfill one of the following criteria: TA NO MO - Deep primary melanoma (>4.0 mm Breslow depth) with or without lymph node involvement; T1-4 N1 MO - Primary melanoma with regional lymph node metastases found at lymphadenectomy, but clinically undetectable (occult); T1-4 N1-2 MO - primary melanoma with clinically apparent (overt) regional lymph node metastases confirmed by lymphadenectomy; or T1-4 N1-2 MO - recurrence of melanoma at the proximal regional lymph node(s) resection. Patients must have an ECOG performance status of 0-1. This is a three arm Phase III study. Patients will be randomized to treatment groups and staged according to the criteria above plus the number of nodes positive at lymphadenectomy. Arm A will be alpha-2 interferon at high dose for one year. Arm B will be alpha-2 interferon at low dose for two years or more. Arm C will consist of observation alone. This study is designed to utilize group sequential analysis procedures to allow multiple comparisons throughout the trial without inflating the Type I error rate. At each planned analysis, two treatment comparisons, one year vs observation and two year vs observation, will be performed using a logrank test stratified by stage of disease. If either one of these primary comparisons crosses the group sequential boundary, then the observation arm may be dropped.

**Progress:** No patients were enrolled at MAMC. This study closed to patient entry 1 June 95.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 92/053		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9119: Primary Chemotherapy of Poor Prognosis Soft Tissue Sarcomas, Phase II					
<b>Start Date:</b> 04/03/92			<b>Est. Completion Date:</b> Mar 95		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Paul C. Sowray, MC					
<b>Associate Investigators:</b>			LTC Howard Davidson, MC		
LTC Luke M. Stapleton, MC			MAJ Kenneth A. Bertram, MC		
MAJ Patrick L. Gomez, MC			MAJ Robert B. Ellis, MC		
MAJ Robert L. Sheffler, MC			CPT Jennifer L. Cadiz, MC		
MAJ Richard C. Tenglin, MC			CPT James S. D. Hu, MC		
<b>Key Words:</b> cancer, soft tissue sarcoma, chemotherapy					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		12/17/93	

**Study Objective:** To evaluate, in patients with high grade soft tissue sarcoma of the extremity, the trunk, or the head and neck, the efficacy of primary chemotherapy, wide surgical resection, adjuvant chemotherapy, and radiotherapy on local control, metastasis free survival, and overall survival; To evaluate the utility of tumor response to primary chemotherapy as an indicator of local and systemic disease control in high grade soft tissue sarcoma; and to evaluate the toxicity of primary chemotherapy, surgery, adjuvant chemotherapy, and radiation therapy in this patient population. Secondary objectives include those listed for SWOG 9136, a companion protocol studying biologic parameters.

**Technical Approach:** Patients with a high grade soft tissue sarcoma of the extremity, trunk, or head and neck area are eligible. Patients will receive chemotherapy using the drugs adriamycin, DTIC, and ifosfamide, given concurrently for three cycles at 21 day intervals. Patients will then undergo wide surgical excision of the primary tumor. Following recovery from surgery, patients with partial or complete response or stable disease will receive another three courses of therapy, followed four weeks after completion of chemotherapy by radiation therapy to the whole area (days 1-5 for 6-8 weeks).

**Progress:** No patients have entered this study at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 93/088	<b>Status:</b> On-going
<b>Title:</b> SWOG 9122: Evaluation of 5-Fluorouracil by Intermittent Infusion in Combination With Alpha-Interferon for Patients with Advanced Renal Cell Carcinoma		
<b>Start Date:</b> 04/02/93	<b>Est. Completion Date:</b> Aug 95	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Timothy P. Rearden, MC		
<b>Associate Investigators:</b>		
MAJ Kenneth A. Bertram, MC	LTC Luke M. Stapleton, MC	
MAJ Mark E. Robson, MC	MAJ Patrick L. Gomez, MC	
CPT Jennifer L. Cadiz, MC	MAJ Robert B. Ellis, MC	
CPT James S. D. Hu, MC	MAJ Richard C. Tenglin, MC	
CPT Diana S. Willadsen, MC	LTC Robert D. Vallion, MC	
<b>Key Words:</b> Cancer:renal cell, 5-FU, alpha-interferon		
<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	12/17/93

**Study Objective:** 1. To evaluate the response rate of advanced renal cell carcinoma to treatment with 5-FU and Alpha-Interferon. 2. To evaluate the toxicities of 5-FU and Alpha-Interferon in this patient population.

**Technical Approach:** Patients with histologically proven renal cell carcinoma which is either metastatic and/or recurrent and bi-dimensionally measurable disease and whose measurements have been provided from x-rays, scans, or physical exam obtained within the past 14 days will be invited to participate in this study.

5-Fluorouracil 750 mg/m<sup>2</sup>/day IV (continuous infusion) on days 1 - 5 q3 weeks and Alpha Interferon 5X10<sup>6</sup> U/m<sup>2</sup> SC on days 1,3,5 q3 weeks will be given. The first dose of interferon will be given at the beginning of 5-FU infusion. The second and third dose may be given in the evening. Pretreatment with acetaminophen 650 mg 1 hour prior to Interferon and as needed to reduce fever will be given.

The 5-FU treatment may be administered as an outpatient using a portable infusion pump capable of delivering the stipulated dosage of 5-FU at a rate of 2 ml per hour. Patients will be evaluated in the clinic weekly by a physician.

**Progress:** One patient was enrolled at MAMC in FY93 and is still being followed. This study closed to patient entry 15 Oct 93.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 93/138	<b>Status:</b> On-going
<b>Title:</b> SWOG 9124: Evaluation of Edatrexate (EDX) in Patients With Relapsed or Refractory Germ Cell Tumors, Phase II		
<b>Start Date:</b> 07/02/93	<b>Est. Completion Date:</b> Aug 98	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Robert B. Ellis, MC		
<b>Associate Investigators:</b>		
LTC Howard Davidson, MC	LTC Luke M. Stapleton, MC	
MAJ Patrick L. Gomez, MC	MAJ Kenneth A. Bertram, MC	
MAJ Mark E. Robson, MC	MAJ Timothy P. Rearden, MC	
CPT James S. D. Hu, MC	MAJ Richard C. Tenglin, MC	
CPT Diana S. Willadsen, MC	LTC Robert D. Vallion, MC	
<b>Key Words:</b> cancer:germ cell, edatrexate		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 12/17/93

**Study Objective:** (1) To assess the rate and duration of response to Edatrexate; (2) to evaluate the patterns of toxicity (qualitative and quantitative) in patients treated with Edatrexate.

**Technical Approach:** Adult patients with relapsed or refractory gonadal or extragonadal germ cell carcinomas will be treated with edatrexate 80 mg/m<sup>2</sup> once weekly for 4 weeks by intravenous bolus injection. After a 1 week rest, patients will be re-treated. One course of therapy consists of 2 cycles (10 weeks) of edatrexate. Therapy will continue until disease progression, unacceptable toxicity or patient withdrawal. Standard response criteria will be utilized to judge response.

**Progress:** One patient was enrolled in FY95 at MAMC and continues to be followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 92/017		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9125: A Phase II Trial of CVAD/Verapamil/Quinine for Treatment of Non-Hodgkin's Lymphoma					
<b>Start Date:</b> 12/06/91			<b>Est. Completion Date:</b> Oct 92		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Patrick L. Gomez, MC					
<b>Associate Investigators:</b>					
MAJ Paul C. Sowray, MC			LTC Howard Davidson, MC		
MAJ Kenneth A. Bertram, MC			LTC Luke M. Stapleton, MC		
MAJ Robert B. Ellis, MC			MAJ Robert L. Sheffler, MC		
CPT Jennifer L. Cadiz, MC			MAJ Richard C. Tenglin, MC		
			CPT James S. D. Hu, MC		
<b>Key Words:</b> cancer, non-Hodgkin's lymphoma, CVAD, verapamil, quinine					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		12/17/93	

**Study Objective:** (1) To evaluate the effectiveness of the CVAD chemotherapy regimen (cyclophosphamide, vincristine, doxorubicin, and dexamethasone) when administered in combination with chemosensitizers (verapamil and quinine) which are intended to block the emergence of multidrug resistance in previously untreated patients with intermediate and high grade non-Hodgkin's lymphoma. The effectiveness of CVAD plus verapamil and quinine will be based on the estimate of the complete response rate and the time to treatment failure. (2) To assess the toxicities and side effects associated with the CVAD regimen when combined with verapamil and quinine. Secondary objectives are to further investigate the utility of the proliferative rate (determined by Ki-67 monoclonal antibody), the importance of cell-cell recognition molecules, the role of host response, and the value of detectable levels of p\_glycoprotein as prognostic indicators of outcome in conjunction with companion study SWOG 8819; and to further utilize the central serum repository enabling clinicopathologic correlations with the results of studies on the material collected (see companion study SWOG 8947).

**Technical Approach:** Currently, regardless of the regimen used, 30 to 60% of advanced stage non-Hodgkin's lymphoma patients will relapse and the emergence of clinical drug resistance is a significant problem in these patients. In this study, patients will receive oral verapamil and quinine on days 1-6 as chemosensitizers. They have been shown to reverse the multidrug resistance associated with P-glycoprotein. Starting on day 2, patients will receive a continuous infusion of Adriamycin and vincristine for four days, Cytosan will be given IV on Day 2 and oral decadron will be given days 2-5. Patients with documented progressive disease at any time will be taken off protocol treatment. Patients with stable disease will receive 2 courses (6 weeks) of chemotherapy. Patients responding to treatment will receive a maximum of 8 courses of chemotherapy. Patients will be restaged upon completion of the treatment program to assess response, with a complete laboratory and radiographic evaluation one month after the completion of therapy. All patients will be followed until death.

**Progress:** This study was closed to patient entry 15 Feb 93. Two patients were enrolled in previous years and are still being followed.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/154		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9126: A Controlled Trial of Cyclosporine as a Chemotherapy-Resistance Modifier in High Risk Acute Myelogenous Leukemia, Phase III					
<b>Start Date:</b> 08/06/93			<b>Est. Completion Date:</b> Sep 94		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Mark E. Robson, MC					
<b>Associate Investigators:</b>					
LTC Howard Davidson, MC			LTC Luke M. Stapleton, MC		
MAJ Kenneth A. Bertram, MC			MAJ Patrick L. Gomez, MC		
MAJ Richard C. Tenglin, MC			MAJ Timothy P. Rearden, MC		
CPT Diana S. Willadsen, MC			CPT James S. D. Hu, MC		
MAJ Richard F. Williams, MC			LTC Robert D. Vallion, MC		
			CPT John R. Caton, MC		
<b>Key Words:</b> cancer:leukemia, cyclosporine, Ara-C, daunorubicin					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		12/17/93	

**Study Objective:** 1. To compare the complete remission rate and duration of survival in patients with high-risk AML when treated with either chemotherapy (Ara-C /Daunomycin) alone or chemotherapy plus the resistance modifier cyclosporine-A (CyA). 2. To estimate the frequency of p-glycoprotein expression and the correlation with prognosis in patients with relapsed AML, primarily refractory AML, and secondary AML.

**Technical Approach:** Patients will be randomized to receive either high-dose Ara-C 3 g/m<sup>2</sup>/d on days 1-5 and daunorubicin 45 mg/m<sup>2</sup>/d on days 6-8, a standard induction regimen for poor-prognosis AML or the same therapy plus cyclosporine A. The cyclosporine A will be given as a loading dose of 6.0 mg/kg IV over 2 hours on day 6 starting 8 hours before the daunorubicin, then 4.0 mg/kg over the next 6 hrs, then 16 mg/kg continuous 24 hr infusion beginning concurrently with the daunorubicin on days 6-8. Bone marrow aspirate and biopsy should be performed on day 14 of induction. Subsequent marrow evaluations should be performed every 7 - 14 days to assess response and recovery period to the next course of chemotherapy.

Patients achieving remission will go on to consolidation. Therapy will consist of the same drugs and dosages except ARA-C will be given on days 1-3 and daunomycin on days 4-6. Cyclosporine A will be given on days 4 - 6 as outlined above. No additional protocol directed treatment will be conducted after consolidation.

**Progress:** One patient was enrolled in this study at MAMC in FY93 and one patient in FY 94. Both are now deceased.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 93/048	<b>Status:</b> Completed
<b>Title:</b> SWOG 9129: Phase III Randomized Study of All-Trans Retinoic Acid Versus Cytosine Arabinoside and Daunorubicin as Induction Therapy for Patients with Previously Untreated Acute Promyelocytic Leukemia		
<b>Start Date:</b> 02/05/93	<b>Est. Completion Date:</b> Jan 96	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Mark E. Robson, MC		
<b>Associate Investigators:</b>		
LTC Howard Davidson, MC	LTC Luke M. Stapleton, MC	
MAJ Patrick L. Gomez, MC	MAJ Kenneth A. Bertram, MC	
MAJ Robert B. Ellis, MC	MAJ Timothy P. Rearden, MC	
MAJ Richard C. Tenglin, MC	CPT Jennifer L. Cadiz, MC	
LTC Robert D. Vallion, MC	CPT James S. D. Hu, MC	
	CPT Diana S. Willadsen, MC	
<b>Key Words:</b> cancer:leukemia, promyelocytic		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 12/17/93

**Study Objective:** The objectives of this study are: (1) to compare the complete remission rate and disease-free survival of all-trans retinoic acid (TRA) to that achieved with conventional remission induction therapy, including cytosine arabinoside (Ara-C) plus daunorubicin (DNR) in patients with previously untreated acute promyelocytic leukemia (APL); (2) to compare the toxicities of TRA to those of Ara-C plus DNR as induction therapy in APL; (3) to determine the value of maintenance therapy with TRA.

**Technical Approach:** Patients with morphologically proven acute promyelocytic leukemia, untreated with radiation therapy or cytotoxic chemotherapy, will be considered for inclusion into this study. This study is designed as a Phase III prospective trial which involves two randomizations. Patients will be initially randomized to either TRA or Daunorubicin plus Cytosine Arabinoside as induction therapy. Consistent with other SWOG studies, one or two cycles of Daunorubicin plus Cytosine Arabinoside will be permitted to achieve complete remission (CR) since approximately 20% of patients not achieving CR with one cycle do so with a second cycle. Following two cycles of consolidation chemotherapy for patients achieving CR, patients will be randomized (second randomization) to either maintenance TRA or observation until relapse. Ancillary laboratory studies will explore biological correlations of TRA responsiveness and the pathophysiology of the coagulopathy.

**Progress:** One patient was enrolled in this study at MAMC in FY93 and is now deceased. This study closed to patient accrual 1 Feb 95.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/097		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9133: Randomized Trial of Subtotal Nodal Irradiation versus Doxorubicin Plus Vinblastine and Subtotal Nodal Irradiation for Stage I-IIA Hodgkin's Disease, Phase III					
<b>Start Date:</b> 05/06/94			<b>Est. Completion Date:</b> Sep 01		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Mark E. Robson, MC					
<b>Associate Investigators:</b>					
LTC Howard Davidson, MC			LTC Luke M. Stapleton, MC		
MAJ Patrick L. Gomez, MC			MAJ Kenneth A. Bertram, MC		
MAJ Robert B. Ellis, MC			MAJ Timothy P. Rearden, MC		
MAJ Richard C. Tenglin, MC			CPT Jennifer L. Cadiz, MC		
LTC Robert D. Vallion, MC			CPT James S. D. Hu, MC		
			CPT Diana S. Willadsen, MC		
<b>Key Words:</b> Cancer:Hodgkin's, irradiation, vinblastine, doxorubicin					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		/ /	

**Study Objective:** The main objective of this study is to compare progression-free and overall survivals of clinically stage (non-laparotomized) patients with early stage (IA,IIA), good-prognosis Hodgkin's Disease treated with either standard subtotal nodal irradiation or with short-course chemotherapy plus standard irradiation. In addition, the study will attempt to identify subgroups of patients who may do better with one approach or the other, and to follow patients for long-term toxicities associated with either regimen.

**Technical Approach:** Patients will be clinically staged by standard methods and then, if they appear to have localized, good-prognosis disease, they will be randomized to receive either standard radiotherapy to mantle and para-aortic fields (subtotal nodal irradiation) or three cycles (6 doses) of chemotherapy followed by the same radiotherapy. Management of both patient groups will be identical apart from the chemotherapy.

**Progress:** Two patients were enrolled in this study, both in FY 94 and continue to be followed.

## Detail Summary Sheet

**Date:** 30 Sep 95      **Protocol No.:** 92/056      **Status:** On-going

**Title:** SWOG 9136: Biologic Parameters in Soft Tissue Sarcomas: A Companion Study to Select Southwest Oncology Group Clinical Trials with Soft Tissue Sarcoma Patients

**Start Date:** 04/03/92      **Est. Completion Date:** Mar 95

**Department:** SWOG      **Facility:** MAMC

**Principal Investigator:** MAJ Paul C. Sowray, MC

<b>Associate Investigators:</b>	LTC Howard Davidson, MC
LTC Luke M. Stapleton, MC	MAJ Kenneth A. Bertram, MC
MAJ Patrick L. Gomez, MC	MAJ Robert B. Ellis, MC
MAJ Robert L. Sheffler, MC	CPT Jennifer L. Cadiz, MC
MAJ Richard C. Tenglin, MC	CPT James S. D. Hu, MC
MAJ George F. Hodeges, MC	

**Key Words:** cancer, soft tissue sarcomas, biologic parameters

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	12/17/93

**Study Objective:** (1) To develop a cooperative group mechanism to study biologic parameters of soft-tissue sarcomas in patients entered onto companion SWOG protocols (see SWOG 9119).; (2) To determine cellular DNA content parameters (DNA CCP) (DNA Ploidy, S-Phase Fraction) of soft tissue sarcomas and to evaluate the effect of these parameters on disease free survival and overall survival. To study the changes in DNA CCP as a result of chemotherapy, and the relationship of these changes to prognosis in patients with soft tissue sarcoma.; (3) To characterize cytogenetic aberrations of soft-tissue sarcomas in the study population. To evaluate the relationship of defined cytogenetic abnormalities to prognosis.; (4) To estimate the level of expression of the multi-drug resistant (MDR) phenotype in untreated soft-tissue sarcoma, and the effect of chemotherapy treatment on the expression of MDR. To evaluate the impact of MDR expression on response to chemotherapy, disease free survival, and overall survival. ; (5) To provide a repository of frozen tissue for future molecular studies in this group of patients.

**Technical Approach:** As a companion protocol to SWOG 9119 (adjuvant soft-tissue sarcoma trial), DNA CCP, tumor karyotypes, and estimation of the expression of the MDR phenotype of sarcomas entered onto trial will be done.

**Progress:** No patients have entered this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 92/054		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9139: Adjuvant Therapy of Primary Osteogenic Sarcomas, Phase II					
<b>Start Date:</b> 04/03/92			<b>Est. Completion Date:</b> Apr 95		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Paul C. Sowray, MC					
<b>Associate Investigators:</b>			LTC Howard Davidson, MC		
LTC Luke M. Stapleton, MC			MAJ Kenneth A. Bertram, MC		
MAJ Patrick L. Gomez, MC			MAJ Robert B. Ellis, MC		
MAJ Robert L. Sheffler, MC			CPT Jennifer L. Cadiz, MC		
MAJ Richard C. Tenglin, MC			CPT James S. D. Hu, MC		
<b>Key Words:</b> cancer, osteogenic sarcoma					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		12/17/93	

**Study Objective:** To estimate the time to treatment failure and survival rate of the three drug combination, Adriamycin, cisplatin, and ifosfamide, as an adjunctive treatment of osteosarcoma of the extremity; to evaluate histopathologic tumor necrosis following preoperative therapy with this regimen; to assess the feasibility of determining histopathologic tumor necrosis in a cooperative group setting; to assess the influence of clinical prognostic variables on disease outcome; and to assess the toxicity of this regimen.

**Technical Approach:** Primary osteosarcoma is an uncommon malignancy but it is associated with only a 20% cure rate, if no more than surgery is used. Chemotherapy increases survival to above 50%, but whether or not this survival could be further increased has to be determined. The current study uses three drugs (Adriamycin, cisplatin, and ifosfamide) in an alternating fashion with the intent of optimizing treatment prior to surgery. Once four cycles of treatment have been completed, surgery will be undertaken. After recovery from surgery, four more cycles of chemotherapy will be given.

**Progress:** No patients have entered this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 93/049	<b>Status:</b> On-going
<b>Title:</b> SWOG 9147: Evaluation of Tamoxifen in Desmoid Tumors, Phase II		
<b>Start Date:</b> 02/05/93	<b>Est. Completion Date:</b> Jan 95	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Diana S. Willadsen, MC		
<b>Associate Investigators:</b>		
LTC Howard Davidson, MC	LTC Luke M. Stapleton, MC	
MAJ Patrick L. Gomez, MC	MAJ Kenneth A. Bertram, MC	
MAJ Mark E. Robson, MC	MAJ Timothy P. Rearden, MC	
CPT Jennifer L. Cadiz, MC	MAJ Robert B. Ellis, MC	
CPT James S. D. Hu, MC	MAJ Richard C. Tenglin, MC	
	LTC Robert D. Vallion, MC	
<b>Key Words:</b> cancer:desmoid tumor		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	12/17/93

**Study Objective:** To assess the response rate of fibromatosis to treatment with tamoxifen. To assess the clonality of fibroblasts using a molecular probe for an x-linked enzyme.

**Technical Approach:** Patients having histologically proven and fully resectable desmoid tumors will be considered for this study. At the time of biopsy, estrogen and progesterone protein assays of the tumor will be done and again at resection. The patient will be placed on Tamoxifen 10 mg PO BID for 6 weeks. At 6 weeks a repeat CT scan or MRI (repeat scan should be the same type as the initial scan) will be done to assess the response. If the objective status at 6 weeks is stable or progressive, surgical excision may proceed. If there is an objective response, treatment will continue another six weeks and after CT scan or MRI excision will proceed. Post-operative or intraoperative radiotherapy will be at the discretion of the treating physician.

Clonality studies will be carried out utilizing restriction fragment length polymorphism techniques with a molecular probe encoding for the enzyme phosphoglycerate kinase. Patients whose tumors would be acceptable for cloning would be "informative females".

If none of the first 20 patients respond to treatment, the study will be closed, and tamoxifen concluded to be inactive. If at least one response is observed, 20 additional patients will be accrued. Five or more responses out of 40 will be considered as evidence warranting further study of tamoxifen.

**Progress:** No patients have been enrolled in this study at MAMC.

## Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 93/089

**Status:** Completed

**Title:** SWOG 9148: A Phase II Study of Cisplatin Preceded by a 12-Hour Continuous Infusion of Concurrent Hydroxyurea and Cytosine Arabinoside ... Extensive Stage Small Cell and Non-small Cell Lung Carcinoma

**Start Date:** 04/02/93

**Est. Completion Date:** Apr 98

**Department:** SWOG

**Facility:** MAMC

**Principal Investigator:** MAJ Timothy P. Rearden, MC

**Associate Investigators:**

LTC Howard Davidson, MC  
MAJ Patrick L. Gomez, MC  
MAJ Robert B. Ellis, MC  
MAJ Richard C. Tenglin, MC  
LTC Robert D. Vallion, MC

LTC Luke M. Stapleton, MC  
MAJ Kenneth A. Bertram, MC  
MAJ Mark E. Robson, MC  
CPT Jennifer L. Cadiz, MC  
CPT James S. D. Hu, MC  
CPT Diana S. Willadsen, MC

**Key Words:** cancer:small cell, cancer:Non-small cell, cisplatin, hydroxyurea, Ara-C, G-CSF

**Accumulative**

**MEDCASE Cost:** \$0.00

**Est. Accumulative**

**OMA Cost:** \$0.00

**Periodic Review:**

12/17/93

**Study Objective:** 1. To evaluate the response rate of this 3-drug program in patients with extensive non-small cell lung cancer. 2. To evaluate the response rate of this program in patients with extensive-stage small cell lung cancer. 3. To assess the qualitative and quantitative toxicities of this regimen in each patient population.

**Technical Approach:** Patients with histologically or cytologically proven disease who have not received prior chemotherapy for lung carcinoma and entering this study will have received blood work and/or other body fluid analyses, x-ray, scans or physical examination used for tumor measurement within the 14 days prior to registration.

Patients will receive allopurinol, 600 mg po, at least 12 hours before start of therapy, and then 300 mg po q.d. continuously until off study. Patients will be hydrated with normal saline, 150 ml/hr or higher rate to maintain urine output  $\geq 100$  cc/hr with intake and output measurements every 4 hours. The hydration must begin at least 8 hours prior to the start of chemotherapy and continue for at least 12 - 24 hours after completion of cisplatin (or until adequate oral intake, whichever is longer). Patients will receive Hydroxyurea  $1260 \text{ mg/m}^2$  in 150 ml 0.9 NS or D5 0.9 NS IVPB over 1 hour via an infusion pump followed immediately by Ara-C  $100 \text{ mg/m}^2$  plus hydroxyurea  $5040 \text{ mg/m}^2$  mixed in the same bag of 1 liter of NS or D5NS and given IVPB over exactly 12 hours using an infusion pump. At the start of the last hour of Ara-C plus hydroxyurea, piggyback Mannitol, 25 gms in 100 ml D5W will be infused into the chemotherapy line over 1 hour. Cisplatin  $100 \text{ mg/m}^2$  in 250 ml NS or D5NS IVPB via an infusion pump will be administered immediately upon completion of the Ara-C, hydroxyurea, and Mannitol. This regimen will be completed every 28 days if absolute granulocytes are  $> 1500$ , platelets are  $> 100,000$ , and measured creatinine clearance  $> 50$ . The treatment should be delayed one week, then a second and third week until these criteria are met. If the parameters are not up to these levels after three 1-week delays the patient will be removed from the study.

**Progress:** There have been no patients enrolled in this study at MAMC. This study closed to patient accrual 1 June 95.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/042		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9152 (EST-4890): Prediction of Recurrence and Therapy Response in Patients with Advanced Germ Cell Tumors by DNA Flow Cytometry					
<b>Start Date:</b> 02/05/93			<b>Est. Completion Date:</b> Jan 95		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Timothy P. Rearden, MC					
<b>Associate Investigators:</b>			LTC Luke M. Stapleton, MC		
LTC Howard Davidson, MC			MAJ Kenneth A. Bertram, MC		
MAJ Patrick L. Gomez, MC			MAJ Mark E. Robson, MC		
MAJ Robert B. Ellis, MC			CPT Jennifer L. Cadiz, MC		
MAJ Richard C. Tenglin, MC			CPT James S. D. Hu, MC		
LTC Robert D. Vallion, MC			CPT Diana S. Walladsen, MC		
<b>Key Words:</b> cancer: germ cell, DNA flow cytometry					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	12/17/93	

**Study Objective:** (1) To determine the proliferative activity and presence of aneuploidy within paraffin-embedded histopathologic specimens from patients with advanced disseminated (poor prognosis) GCT; (2) to correlate proliferative activity and aneuploidy with clinical features including response to therapy, relapse-free survival, and overall survival in patients entered on ECOG protocol EST 3887/SWOG 8997/CALGB 8991; Phase III Chemotherapy of Disseminated Advanced Stage Testicular Cancer with Cisplatin plus Etoposide with either Bleomycin or Isosfamide.

**Technical Approach:** All pathologic materials will be obtained during the routine diagnostic evaluation of patients registered on EST 3887/SWOG 8997 CALGB 8991. Following pathologic analysis of blocks to determine adequacy of tissue, tissue will be prepared for flow cytometry analysis. Three 50 micron sections will be cut, deparaffinized and rehydrated, enzymatically digested, and stained with the DNA intercalating agent propidium iodide. The florescence of propidium iodide-stained nuclei will be measured on a Coulter 753 tunable dye laser following filtration through a 53 micron nylon mesh. Evaluation of the DNA index (ploidy status) and proliferative activity (cell cycle compartment analysis and proliferative index) will then proceed.

**Progress:** Two patients were enrolled in FY93. One patient is still be followed and the other died of the disease. This study closed to patient accrual 1 Feb 95.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/063	<b>Status:</b> On-going
<b>Title:</b> SWOG 9158: A Phase II Evaluation of Trans-Retinoic Acid and Alpha Interferon in Patients with Squamous Cell Carcinoma of the Lung (Stage IV)		
<b>Start Date:</b> 02/04/94	<b>Est. Completion Date:</b> Feb 98	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Timothy P. Rearden, MC		
<b>Associate Investigators:</b>		
LTC Howard Davidson, MC	LTC Luke M. Stapleton, MC	
MAJ Patrick L. Gomez, MC	MAJ Kenneth A. Bertram, MC	
MAJ Robert B. Ellis, MC	MAJ Mark E. Robson, MC	
CPT James S. D. Hu, MC	MAJ Richard C. Tenglin, MC	
CPT Diana S. Willadsen, MC	LTC Robert D. Vallion, MC	
	MAJ Richard F. Williams, MC	
<b>Key Words:</b> Cancer:lung, trans-retinoic acid, alpha interferon		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objective:** 1) To assess the response rate to trans-Retinoic Acid and Alpha Interferon used in a daily schedule for patients with advanced (TNM Stage IV), well differentiated squamous cell carcinoma of the lung. 2) To further define the qualitative and quantitative toxicities of this regimen administered to this patient population in a Phase II study.

**Technical Approach:** Patients with a histologically confirmed diagnosis of advanced, well differentiated squamous cell carcinoma of the lung will be invited to participate in this evaluation of trans-Retinoic Acid and Alpha Interferon for the treatment of Stage IV Squamous Cell Carcinoma of the lung. After baseline evaluation, patients will be started on a fixed dose of trans-Retinoic Acid, 150 mg/m<sup>2</sup>/d P.O. in divided doses (b.i.d.) with meals and 3 X 10<sup>6</sup> I.U./m<sup>2</sup> of Roferon-A subcutaneously once daily for 5 day/week. Measurable disease will be assessed for response or progression by chest x-ray at least every four weeks and CT scan (if needed) every 8 weeks. Patients will continue to receive therapy until they have stable disease after 16 weeks of therapy, one year after documentation of complete response, two years after documentation of a partial response, disease progression, relapse, or toxicity. All patients will be followed until death. Data will be interpreted by sponsors.

**Progress:** One patient was enrolled in FY95 at MAMC and continues to be followed.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 93/097	<b>Status:</b> On-going
<b>Title:</b> SWOG 9205: Central Prostate Cancer Serum Repository Protocol		
<b>Start Date:</b> 05/07/93	<b>Est. Completion Date:</b> Mar 95	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Timothy P. Rearden, MC		
<b>Associate Investigators:</b>		
MAJ Kenneth A. Bertram, MC	LTC Luke M. Stapleton, MC	
MAJ Mark E. Robson, MC	MAJ Patrick L. Gomez, MC	
CPT Jennifer L. Cadiz, MC	MAJ Robert B. Ellis, MC	
CPT James S. D. Hu, MC	MAJ Richard C. Tenglin, MC	
CPT Diana S. Willadsen, MC	LTC Robert D. Vallion, MC	
<b>Key Words:</b> Cancer:prostate, serum repository		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 12/17/93

**Study Objective:** 1. To store serum of patients with confirmed adenocarcinoma of the prostate entered onto clinical trials conducted by the SWOG Genitourinary Committee. 2. To provide the serum of the above patients entered onto SWOG studies for specific clinical-laboratory investigations outlined on separate SWOG protocols approved by the Genitourinary Committee Tumor Biology Subcommittee.

**Technical Approach:** This serum bank is to provide the opportunity for study of new or existing markers or other tests in a prospective or retrospective fashion, in order to test their usefulness as diagnostic or management tools in prostate cancer at all stages. Specific information regarding the nature of individual tests to be conducted on the serum samples of these patients will be described in individual protocols.

All serum samples (approx. 3 - 5 cc) will be collected from patients in the frequency and timing indicated on specific protocols. Samples will be spun 15 minutes after collection and stored at a minimum of -20 C. Samples will be frozen and shipped to the Serum Bank Coordinator.

**Progress:** Two patients were enrolled in this serum study (1 in FY95). Both continue to be followed.

### Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 94/115

**Status:** On-going

**Title:** SWOG 9208: Health Status and Quality of Life in Patients With Early Stage Hodgkin's Disease: A Companion Study to SWOG 9133

**Start Date:** 06/03/94

**Est. Completion Date:** Jun 98

**Department:** SWOG

**Facility:** MAMC

**Principal Investigator:** CPT James S. D. Hu, MC

**Associate Investigators:**

LTC Howard Davidson, MC  
MAJ Patrick L. Gomez, MC  
MAJ Mark E. Robson, MC  
MAJ Richard C. Tenglin, MC  
CPT Diana S. Willadsen, MC

LTC Luke M. Stapleton, MC  
MAJ Kenneth A. Bertram, MC  
MAJ Timothy P. Rearden, MC  
MAJ Robert B. Ellis, MC  
LTC Robert D. Vallion, MC  
MAJ Richard F. Williams, MC

**Key Words:** Cancer:Hodgkin's, quality of life

**Accumulative**

**MEDCASE Cost:** \$0.00

**Est. Accumulative**

**OMA Cost:** \$0.00

**Periodic Review:**

//

**Study Objective:** 1) To evaluate prospectively the health status and quality of life (QOL) of early stage Hodgkin's Disease patients receiving either subtotal nodal irradiation or short course chemotherapy plus subtotal nodal irradiation. 2) To describe the short-term, acute effects of two treatments for early stage Hodgkin's Disease patients on patient report of symptoms and on patient QOL. 3) To evaluate the intermediate and long-term effects of two treatments for early stage Hodgkin's Disease patients on patient QOL over five years.

**Technical Approach:** Patients enrolled in the companion protocol, SWOG-9133, will be asked to complete questionnaires before registration into this study, at 6 months; and annually for seven years. These questionnaires seek to identify and quantitate those differences pertaining to quality of life issues that the added chemotherapy may have in early stage Hodgkin's disease patients.

**Progress:** No patients have been enrolled in this study.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 93/107	<b>Status:</b> On-going
<b>Title:</b> SWOG 9210: A Phase III Randomized Trial of Combination Therapy for Multiple Myeloma Comparison of (1) VAD-P to VAD-P/Quinine for Induction; (2) Randomization of Prednisone Dose Intensity for ....		
<b>Start Date:</b> 05/07/93	<b>Est. Completion Date:</b> May 98	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT James S. D. Hu, MC		
<b>Associate Investigators:</b>		
MAJ Kenneth A. Bertram, MC	LTC Luke M. Stapleton, MC	
MAJ Timothy P. Rearden, MC	MAJ Patrick L. Gomez, MC	
MAJ Robert B. Ellis, MC	MAJ Mark E. Robson, MC	
MAJ Richard C. Tenglin, MC	CPT Jennifer L. Cadiz, MC	
CPT Diana S. Willadsen, MC	LTC Robert D. Vallion, MC	
<b>Key Words:</b> Cancer:myeloma, VAD-P, VAD-P,Quinine		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 12/17/93

**Study Objective:** (1) To compare the effectiveness of the VAD-P chemotherapy regimen when administered alone or in combination with the chemosensitizer quinine intended to block the emergence of multidrug resistance during remission induction in previously untreated patients with multiple myeloma; (2) To evaluate the chemosensitizing potential of quinine to reverse drug resistance in myeloma patients randomized to VAD-P induction who fail to achieve at least 25% regression with chemotherapy alone. 3. To compare the value of alternate day prednisone 10 mg versus 50 mg for remission maintenance for patients proven to achieve at least 25% regression.

**Technical Approach:** Patients with proven multiple myeloma (all stages) who have not received prior chemotherapy are eligible for participation in this trial. A dynamic allocation scheme will be used to randomize patients to one of the two induction treatment arms.

**INDUCTION:** ARM I patients will receive Vincristine 0.4 mg IV q.d. on days 1-4, Doxorubicin 9 mg/m<sup>2</sup> q.d. IV on days 1-4, Dexamethasone 40 mg q.d. PO on days 1-4, and Prednisone 50 mg Q.O.D. on days 9, 11, 13, 15, 17, and 19. This cycle will be repeated Q 21 days for a minimum of 6 to 8 cycles (6 months) or a maximum of 17 cycles (12 months). Patients who fail to achieve  $\geq 25\%$  tumor regression after 12 months of treatment on Arm I (VAD-P) or relapse or progress on Arm I, will be eligible for crossover to VAD-P/Q.

ARM II and Crossover schedule patients will receive VAD-P as outlined above on days 2-5 and will also receive Quinine 400 mg t.i.d. on days 1-6 (VAD-P/Q).

Patients with  $\geq 25\%$  tumor regression after 9 to 12 months of induction therapy or patients who achieve  $\geq 50\%$  tumor regression after 6 months of induction therapy will be randomized to either of two maintenance regimens. If, in the judgement of the physician the patient will continue to benefit from induction therapy, they may continue up to 12 months.

**MAINTENANCE:** ARM III patients will receive Prednisone, 10 mg Q.O.D., until relapse and ARM IV patients will receive Prednisone 50 mg Q.O.D. until relapse.

**Progress:** One patient has been enrolled (FY94) and continues to be followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/090		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9216: A Randomized Phase III Study of CODE Plus Thoracic Irradiation Versus Alternating CAV and EP for Extensive Stage Small Cell Lung Cancer					
<b>Start Date:</b> 04/02/93			<b>Est. Completion Date:</b> Mar 98		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Timothy P. Rearden, MC					
<b>Associate Investigators:</b>					
LTC Howard Davidson, MC			LTC Luke M. Stapleton, MC		
MAJ Patrick L. Gomez, MC			MAJ Kenneth A. Bertram, MC		
MAJ Robert B. Ellis, MC			MAJ Mark E. Robson, MC		
MAJ Richard C. Tenglin, MC			CPT Jennifer L. Cadiz, MC		
LTC Robert D. Vallion, MC			CPT James S. D. Hu, MC		
			CPT Diana S. Willadsen, MC		
<b>Key Words:</b> Cancer:lung, cisplatin, adriamycin, vincristine, etoposide, cyclophosphamide, irradiation					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		12/17/93	

**Study Objective:** To determine if chemotherapy dose intensification and thoracic irradiation will improve the response rate and overall survival rate in patients with extensive small cell lung cancer.

**Technical Approach:** Patients with extensive, measurable or evaluable disease will be randomized to 1 of 2 arms. Those randomized to Arm 1 will receive CODE (cisplatin, vincristin, doxorubicin, and etoposide) administered as follows: Cisplatin 25 mg/m<sup>2</sup> IV over 15 minutes weekly; Vincristine 1 mg/m<sup>2</sup> IV over 15 minutes weeks 1, 2, 6, 8; Doxorubicin 40 mg/m<sup>2</sup> IV over at least 10 minutes weeks 1, 3, 5, 7, 9; Etoposide 80 mg/m<sup>2</sup> IV over 20 - 30 minutes day 1 of weeks 1, 3, 5, 7, 9 and Etoposide 80 mg/m<sup>2</sup> PO days 2 & 3 of weeks 1, 3, 5, 7, 9. Those randomized to Arm 2 will receive alternating CAV/EP scheduled as follows: Cyclophosphamide 100 mg/m<sup>2</sup> IV 100 mg every 1 - 2 minutes of weeks 1, 7, 13; Doxorubicin 50 mg/m<sup>2</sup> IV over at least 10 minutes on day 1 of weeks 1, 7, 13; and Vincristine 1.2 mg/m<sup>2</sup> IV over 2 - 3 minutes day 1 of weeks 1, 7, 13 and Etoposide 100 mg/m<sup>2</sup> IV over 20 - 30 minutes days 1, 2 & 3 of weeks 4, 10, 16; Cisplatin 25 mg/m<sup>2</sup> VI over 15 minutes days 1, 2, & 3 of weeks 4, 10, 16. Supportive drugs (corticosteroid, gastroprotective agent, antifungal agent, prophylactic antibiotic Colony-stimulating factor, will be given according to set criteria.

After complete protocol cytotoxic chemotherapy, all patients will be re-staged, with repeat of any investigation that was abnormal prior to entry. If a patients should refuse re-staging, but appears on the available evidence to be in complete response, prophylactic cranial irradiation may be offered at the discretion of the investigator.

Patients on ARM 1 who achieve a complete response or partial response at the primary site with a complete response at all known metastatic sites will receive both thoracic irradiation to the mediastinum and site of the primary and prophylactic cranial irradiation beginning 3 to 4 weeks after completion of systemic therapy. These may be given concurrently and are obligatory.

Patients on Arm II who achieve a complete response will receive at least prophylactic cranial irradiation and this is obligatory. Other radiation therapy for patients in this arm is non-obligatory but may be given at the discretion of the investigator and should begin 3 to 4 weeks after completion of systemic therapy.

Progression-free survival will be compared between treatment arms. Generalized Wilcoxon and log-rank statistics will be used to compare survival experience between the two arms. A Cox proportional hazards model will be used to assess prognostic factors, and treatment effect will be tested after controlling for important prognostic variables. Response rates and toxicities between the two treatment arms will be compared by Fisher's exact test. Logistic regression will be used to assess and adjust for prognostic factors with respect to complete response.

Some patients responding to the CODE regimen will not be able to continue the weekly chemotherapy because of unacceptable constitutional toxicity or patient refusal. These patients should be offered the standard regimen (alternating CAV and EP) as they may be able to tolerate a chemotherapy program allowing sufficient time between treatments to convalesce from side effects.

Progress: One patient enrolled in FY95 at MAMC and continues to be followed.

### Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 94/010

**Status:** On-going

**Title:** SWOG 9217: Chemoprevention of Prostate Cancer with Finasteride (Proscar), Phase III, Intergroup

**Start Date:** 10/01/93

**Est. Completion Date:**

**Department:** SWOG

**Facility:** MAMC

**Principal Investigator:** MAJ J. Brantley Thrasher, MC

**Associate Investigators:** None

**Key Words:** Cancer: prostate, Finasteride

**Accumulative**

**Est. Accumulative**

**Periodic Review:**

**MEDCASE Cost:** \$0.00

**OMA Cost:** \$0.00

09/21/94

**Study Objective:** The primary objective of this trial will be to determine if finasteride can reduce the development of prostatic cancer in males 55 years and older.

**Technical Approach:** Men who have attained 55 years of age have never been diagnosed as having prostatic cancer will be randomized to receive Finasteride 5 mg or Matched Placebo PO daily for 7 years. Patients will be followed with clinic visits at 6 months, 1 year and then annually. Annual laboratory screening will include PSA. Triggers are in place to initiate prostatic biopsies. The final endpoint is biopsy proven presence/absence of carcinoma of the prostate after seven years.

**Progress:** 26 patients have been enrolled in this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/023	<b>Status:</b> On-going
<b>Title:</b> SWOG 9219: A Phase II Evaluation of Interleukin-4 (IL-4) in Patients With Non-Hodgkin's Lymphoma or Hodgkin's Disease		
<b>Start Date:</b> 11/18/94	<b>Est. Completion Date:</b> Nov 98	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT James S. D. Hu, MC		
<b>Associate Investigators:</b>		
LTC Howard Davidson, MC	LTC Luke M. Stapleton, MC	
MAJ Timothy P. Rearden, MC	MAJ Kenneth A. Bertram, MC	
LTC Robert D. Vallion, MC	MAJ Robert B. Ellis, MC	
MAJ Richard F. Williams, MC	CPT Diana S. Willadsen, MC	
	CPT John R. Caton, MC	
<b>Key Words:</b> Cancer:Hodgkin's, Cancer:Non-Hodgkin's, Interleukin-4		
<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	//

**Study Objective:** 1) To assess the response rate of refractory low grade non-Hodgkin's lymphoma, refractory intermediate or high grade non-Hodgkin's lymphoma and refractory Hodgkin's disease treated with interleukin-4, and 2) to assess the qualitative and quantitative toxicities of interleukin-4 administered in a Phase II study.

**Technical Approach:** Following pretreatment with acetaminophen (650 mg PO) to prevent chills and fever, patients will receive a subcutaneous injection of interleukin-4 (at an initial dose of 3 ug/kg daily for 28 days). Patients must be observed in a medical facility for at least 2 hours after the first 2 daily injections. If no significant side effects occur the patient or family member will be instructed on how to administer subsequent injections at home. Patients will be reevaluated after 28 days with a possible rest period of one or two weeks between 28 day cycles of this treatment.

**Progress :** No patients have been enrolled at MAMC.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 93/136		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9221, MDACC ID 91-025, INT-191-001: Phase III Double-Blind Randomized Trial of 13-Cis Retinoic Acid (13-cRA) to Prevent Second Primary Tumors (SPTs) in Stage I Non-Small Cell Lung Cancer					
<b>Start Date:</b> 07/02/93			<b>Est. Completion Date:</b> Jul 98		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Timothy P. Rearden, MC					
<b>Associate Investigators:</b>					
LTC Howard Davidson, MC			LTC Luke M. Stapleton, MC		
MAJ Patrick L. Gomez, MC			MAJ Kenneth A. Bertram, MC		
MAJ Robert B. Ellis, MC			MAJ Mark E. Robson, MC		
MAJ Richard C. Tenglin, MC			CPT Jennifer L. Cadiz, MC		
LTC Robert D. Vallion, MC			CPT James S. D. Hu, MC		
			CPT Diana S. Willadsen, MC		
<b>Key Words:</b> cancer:non-small cell lung, 13-cis retinoic acid					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>		
\$0.00		\$0.00	12/17/93		

**Study Objective:** To evaluate: (1) the efficacy of 13-cis-retinoic acid (13-cRA) in reducing the incidence of SPTs in patients who have been treated for Stage I non-small cell lung cancer with complete surgical resection; (2) the qualitative and quantitative toxicity of 13-cRA in a daily administration schedule; and (3) compare the overall survival of patients treated with 13-cRA vs. patients treated with placebo.

**Technical Approach:** Patients enrolling into this study will be stratified according to histology, T stage and smoking status then registered into a Single-Blind, 8 week run-in period to test compliance. All patients will receive placebo during this period. After Run-in the patients will be randomized into a double-blind trial to receive 13-cRA (30 mg p.o./d x 3 yrs vs. Placebo (30 mg p.o./d x 3 yrs). Each group will have a 4 year follow-up period.

The final analysis will be undertaken shortly after seven years. The primary hypothesis for the study is whether 13-cRA lowered the rate of second primary tumors (SPT). All patients randomized will be grouped according to the assigned treatment. Patients who are either purely lost to follow up or died without a SPT occurring will be included in the actuarial analysis with a censored status on the last day of contact. The primary hypothesis of treatment benefit will be tested using the proportional hazards model.

**Progress:** Five patients have been enrolled in this study at MAMC (3 in FY95). All continue to be followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/064		<b>Status:</b> Completed	
<b>Title:</b> SWOG 9223: Evaluation of Trans-Retinoic Acid Plus Alpha Interferon in Stage IV Melanoma					
<b>Start Date:</b> 02/04/94			<b>Est. Completion Date:</b> Feb 97		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Richard C. Tenglin, MC					
<b>Associate Investigators:</b>					
LTC Howard Davidson, MC			LTC Luke M. Stapleton, MC		
MAJ Patrick L. Gomez, MC			MAJ Kenneth A. Bertram, MC		
MAJ Mark E. Robson, MC			MAJ Timothy P. Rearden, MC		
CPT James S. D. Hu, MC			MAJ Robert B. Ellis, MC		
CPT Diana S. Willadsen, MC			LTC Robert D. Vallion, MC		
			MAJ Richard F. Williams, MC		
<b>Key Words:</b> Cancer:melanoma, trans-retinoic acid, alpha interferon					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		/ /	

**Study Objective:** 1) To evaluate the response rate in patients with melanoma treated with a combination of all trans-Retinoid Acid and Alpha Interferon. 2) To evaluate the qualitative and quantitative toxicities of the combination of all trans-Retinoic Acid and Alpha Interferon.

**Technical Approach:** Patients enrolled in this study must have a histologically proven diagnosis of malignant melanoma with metastatic disease. All patients will receive trans-retinoic acid 37.5 mg/m<sup>2</sup> b.i.d. orally with meals for three weeks followed by one week of rest. Alpha interferon will be given as a subcutaneous injection every Monday, Wednesday, and Friday continuously while the patient is on protocol treatment. There is no rest period for interferon administration. If the trans-retinoic acid is well tolerated after the first course, it will be dose escalated to 75 mg/m<sup>2</sup>. One course of therapy consists of 4 weeks. Patients will remain on therapy until evidence of progression occurs or other criteria for removal are met. All patients will be followed until death.

**Progress:** No patients have been enrolled in this study at MAMC. This study closed to patient accrual 15 Aug 95.

### Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 93/108

**Status:** On-going

**Title:** SWOG 9237: Evaluation of Topotecan in Refractory and Relapsing Multiple Myeloma

**Start Date:** 05/07/93

**Est. Completion Date:** May 98

**Department:** SWOG

**Facility:** MAMC

**Principal Investigator:** CPT James S. D. Hu, MC

**Associate Investigators:**

LTC Howard Davidson, MC  
MAJ Patrick L. Gomez, MC  
MAJ Mark E. Robson, MC  
CPT Jennifer L. Cadiz, MC  
LTC Robert D. Vallion, MC

LTC Luke M. Stapleton, MC  
MAJ Kenneth A. Bertram, MC  
MAJ Timothy P. Rearden, MC  
MAJ Robert B. Ellis, MC  
MAJ Richard C. Tenglin, MC  
CPT Diana S. Willadsen, MC

**Key Words:** Cancer: myeloma; topotecan

**Accumulative  
MEDCASE Cost:**

\$0.00

**Est. Accumulative  
OMA Cost:**

\$0.00

**Periodic Review:**  
12/17/93

**Study Objective:** (1) To evaluate the response rate for refractory myeloma treated with topotecan; (2) To evaluate the qualitative and quantitative toxicities of topotecan administered in a Phase II study; (3) To measure topoisomerase levels in multiple myeloma cells.

**Technical Approach:** Patients with proven multiple myeloma, with protein criteria present, who have received exactly one prior regimen, and have shown, in the opinion of the investigator, to have disease progression are eligible for this study. All patients will receive topotecan 1.25 mg/m<sup>2</sup> q.d. IV over 30 minutes on days 1-5 repeated q 21 days. This schedule will continue as long as patients show complete remission, partial remission or stable disease and toxicity is acceptable. Topotecan dosage can be adjusted on nadir counts of the preceding cycle.

It is assumed that topotecan will be of interest if a true response rate of 20% or more is achieved in the treatment of patients with relapsed or refractory multiple myeloma.

**Progress:** One patient was entered in this study in FY93 and continues to be followed. This study closed to patient accrual 15 Feb 95.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 93/092	<b>Status:</b> On-going
<b>Title:</b> SWOG 9245: Central Lymphoma Repository Tissue Procurement Protocol for Relapse or Recurrent Disease		
<b>Start Date:</b> 04/02/93	<b>Est. Completion Date:</b> May 95	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Mark E. Robson, MC		
<b>Associate Investigators:</b>		
LTC Howard Davidson, MC	LTC Luke M. Stapleton, MC	
MAJ Patrick L. Gomez, MC	MAJ Kenneth A. Bertram, MC	
MAJ Robert B. Ellis, MC	MAJ Timothy P. Rearden, MC	
MAJ Richard C. Tenglin, MC	CPT Jennifer L. Cadiz, MC	
CPT Diana S. Willadsen, MC	CPT James S. D. Hu, MC	
	LTC Robert D. Vallion, MC	
<b>Key Words:</b> cancer:lymphoma, tissue procurement		
<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	12/17/93

**Study Objective:** 1. To acquire fresh snap-frozen lymphoma tissue from patients who relapse or have recurrent disease after being treated on Southwest Oncology Group treatment protocols. 2. To establish a standard set of procedures for routine acquisition, banking, and study of lymphoma tissues within the cooperative group. 3. To use the repository tissue to establish clinical correlations via presently activated phenotyping studies and future projected molecular studies assessing specimen DNA and RNA status. 4. To examine the biology of therapy failure in relationship to changes in pretreatment and post-therapy immunophenotypic data.

**Technical Approach:** Fresh frozen tissues will be acquired from relapsed patients for basic science protocols, both current and future, designed to better define the biology of relapsed non-Hodgkins's lymphoma. This is not a treatment protocol, nor will results be used to guide treatment decisions.

Fresh biopsies (from any organ site) will be snap-frozen and submitted with one stained (Hematoxylin and Eosin) histologic section with accompanying pathology report to The Department of Pathology at the University of Arizona in Tucson.

**Progress:** No patients have entered this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 93/110	<b>Status:</b> On-going
<b>Title:</b> SWOG 9246: A Phase II Evaluation of Taxol in Patients with Relapsed Non-Hodgkin's Lymphoma or Relapsed Hodgkin's Disease		
<b>Start Date:</b> 05/07/93	<b>Est. Completion Date:</b> Jun 94	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Mark E. Robson, MC		
<b>Associate Investigators:</b>		
LTC Howard Davidson, MC	LTC Luke M. Stapleton, MC	
MAJ Kenneth A. Bertram, MC	MAJ Patrick L. Gomez, MC	
CPT Jennifer L. Cadiz, MC	MAJ Timothy P. Rearden, MC	
CPT James S. D. Hu, MC	MAJ Robert B. Ellis, MC	
LTC Robert D. Vallion, MC	MAJ Richard C. Tenglin, MC	
	CPT Diana S. Willadsen, MC	
<b>Key Words:</b> Cancer:Hodgkin's, Cancer:non-Hodgkin's, taxol		
<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	12/17/93

**Study Objective:** (1) To assess the response rate of relapsed low-grade non-Hodgkin's lymphoma, relapsed intermediate or high-grade non-Hodgkin's lymphoma, and relapsed Hodgkin's disease treated with taxol; (2) To assess the qualitative and quantitative toxicities of taxol administered in a phase II trial.

**Technical Approach:** All participants of this study must have a biopsy proven diagnosis of low, intermediate or high grade malignant non-Hodgkin's lymphoma or Hodgkin's disease and have received prior therapy. Participants will be stratified by type of disease: low grade lymphoma, intermediate or high grade lymphoma and Hodgkin's Disease. In an effort to avoid acute allergic reactions, all patients will be premedicated with Dexamethasone, Diphenhydramine, and Cimetidine prior to the administration of Taxol. The initial dose of Taxol will be 175 mg/m<sup>2</sup> for all patients except it will be 135 mg/m<sup>2</sup> for those who have received prior radiotherapy to 30% or more of marrow-bearing bone. Therapy will be administered only to inpatients and dosage may be modified for toxicities.

Estimates of response and toxicity will be made for each disease category separately. A response probability of 35% would be of interest, while further testing of this regimen would not be pursued if the response probability was 15% or lower.

**Progress:** No patients have entered this study at MAMC.

## Detail Summary Sheet

**Date:** 30 Sep 95      **Protocol No.:** 94/161      **Status:** On-going

**Title:** SWOG 9250 (INT-0136): Phase III Intergroup Prospectively Randomized Trial of Perioperative 5-FU After Curative Resection, Followed by 5-FU/Levamisole for Patients With Colon Cancer

**Start Date:** 09/21/94      **Est. Completion Date:** Sep 98

**Department:** SWOG      **Facility:** MAMC

**Principal Investigator:** MAJ Robert B. Ellis, MC

<b>Associate Investigators:</b>	LTC Luke M. Stapleton, MC
LTC Howard Davidson, MC	MAJ Kenneth A. Bertram, MC
MAJ Timothy P. Rearden, MC	CPT James S. D. Hu, MC
LTC Robert D. Vallion, MC	CPT Diana S. Willadsen, MC
MAJ Richard F. Williams, MC	CPT John R. Caton, MC

**Key Words:** Cancer:colon, resection, chemotherapy:perioperative, 5FU, levamisole

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	//

**Study Objective:** To determine if (1) adjuvant therapy with one week of continuous 5-FU given within 24 hours of a curative colon resection followed by 12 months of 5-FU/Levamisole is effective in prolonging the disease free interval and increasing survival in patients who are treated with 5-FU/Levamisole only. Endpoints include: treatment failure - as described by recurrence of local/regional or distant metastases - and survival. (2) To establish within ECOG a Central Tissue Repository for paraffin blocks and a frozen tissue bank.

**Technical Approach:** Patients with primary colon cancer will be randomized to either receive 7 days of continuous intravenous 5-fluorouracil (5-FU) within 24 hours completion of colon surgery or not to receive any perioperative chemotherapy.

The only investigational part of this protocol is the administration of chemotherapy during the period right after subjects colon operation. The operation and the use of 5-FU/levamisole are all standard treatment.

**Progress:** No patients have been enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/105	<b>Status:</b> On-going
<b>Title:</b> SWOG 9252: Prospective Randomized Trial of Postoperative Adjuvant Therapy in Patients with Completely Resected Stage II and Stage IIIa Non-small Cell Lung Cancer, Intergroup		
<b>Start Date:</b> 05/06/94	<b>Est. Completion Date:</b> May 98	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Timothy P. Rearden, MC		
<b>Associate Investigators:</b>		
LTC Howard Davidson, MC	LTC Luke M. Stapleton, MC	
MAJ Patrick L. Gomez, MC	MAJ Kenneth A. Bertram, MC	
MAJ Robert B. Ellis, MC	MAJ Mark E. Robson, MC	
CPT James S. D. Hu, MC	MAJ Richard C. Tenglin, MC	
CPT Diana S. Willadsen, MC	LTC Robert D. Vallion, MC	
	MAJ Richard F. Williams, MC	
<b>Key Words:</b> Cancer:lung, non-small cell, cisplatin, etoposide		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> / /

**Study Objective:** 1) To determine if combination chemotherapy plus thoracic radiotherapy is superior to thoracic radiotherapy alone in prolonging survival in patients with completely resected Stage II and IIIa non-small cell lung cancer. 2) To determine if combination chemotherapy plus thoracic radiotherapy is superior to thoracic radiotherapy alone in preventing local recurrence in patients with resected Stage II or IIIa non-small cell lung cancer.

**Technical Approach:** Patients who have undergone a surgery for Stage II or IIIa disease are eligible to participate in this trial. Patients will be stratified for nodal status (N1, N2), histology (squamous, other), weight loss in previous 6 months (< 5%, >= 5%), and lymph node dissection (sampling, complete node resection). After stratification they will be randomized to receive radiotherapy treatment (50.4 Gy/28 fractions/6 weeks) alone or radiotherapy treatment (50.4 Gy/28 fractions/6 weeks) concurrent with Cisplatin (DDP) 60 mg/m<sup>2</sup> IV days 1, 29, 57, 85 and Etoposide (VP-16) 120 mg/m<sup>2</sup> IV days 1, 2, 3; 29, 20, 31; 57, 58, 59; 85, 86, 87. Patients will be followed for 5 years. The statistical analysis will be based mainly on the stratified logrank test for comparison of two treatments. The second endpoint of local recurrence rate will be also analyzed as will the time to recurrence.

**Progress:** One patient has been enrolled in this study at MAMC in FY95 and continues to be followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/073	<b>Status:</b> On-going
<b>Title:</b> SWOG 9300: A Randomized Phase II Evaluation of All Trans-Retinoic Acid with Interferon-Alfa 2a or All Trans-Retinoic Acid with Hydroxyurea.... Diagnosed Chornic Myelogenous Leukemia in Chronic Phase		
<b>Start Date:</b> 03/04/94	<b>Est. Completion Date:</b> Mar 94	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Mark E. Robson, MC		
<b>Associate Investigators:</b>		
LTC Howard Davidson, MC	LTC Luke M. Stapleton, MC	
MAJ Patrick L. Gomez, MC	MAJ Kenneth A. Bertram, MC	
MAJ Robert B. Ellis, MC	MAJ Timothy P. Rearden, MC	
CPT James S. D. Hu, MC	MAJ Richard C. Tenglin, MC	
CPT Diana S. Willadsen, MC	LTC Robert D. Vallion, MC	
	MAJ Richard F. Williams, MC	
<b>Key Words:</b> Cancer:leukemia, chronic myelogenous, trans-retinoic acid, alpha interferon, hydroxyurea		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$9686.00	<b>Periodic Review:</b> / /

**Study Objective:** 1). To estimate whether treatment of Chronic Myelogeneous Leukemia (CML), with all-trans retinoic acid in combination with either hydroxyurea or interferon alfa-2a is sufficiently effective based on either hematologic or cytogenetic response, to justify its investigation in phase III trials. 2). To assess the toxicities associated with all-trans retinoic acid plus hydroxyurea or itnerferon alfa-2a in chronic phase CML.

**Technical Approach:** Patients qualifying for this study will be stratified by age (< 45 vs >=45), splenomegaly (present vs absent), prior hydroxyurea (yes or no), and ANC at diagnosis (<50,000 ul). Patients will then be randomized to one of two treatment arms as follows: Arm I: ATRA and HU or Arm II: ATRA and IFN. This randomization will be dynamically balanced to assure roughly equal numbers of patients within levels of the stratifying factors.

All patients in both arms will begin treatment with HU to control or keep the WBC  $\leq 20,000/\text{ul}$  and platelets  $\leq 800,000/\text{ul}$ . All therapy will include allopurinol. Patients will receive this HUS treatment for a minimum of 21 days and a maximum of 42 days. Patients with WVA  $\leq 20,000/\text{ul}$ , platelets  $\leq 800,00/\text{ul}$ , and no evidence of progressive splenomegaly after 21 - 42 days of HU will then bergin treatment on their assigned regimens. Patients who do not achieve a WBC  $\leq 20,000/\text{ul}$ , platelets  $\leq 800,000/\text{ul}$ , and absence of progressive splenonegaly after 42 days will be removed from protocol treatment. Arm I patients will receive ATRA 150/mg/m<sup>2</sup>/d x 7 days followed by 7 days rest and HU 500 mg qd adjusted to maintain WBC and platelets to predefined levels. Arm II patients will receive acetaminophen 650 mg 1/2 hr before administration of IFN initiated a 3 MIU/m<sup>2</sup>/d 5 days/week escalated by 1 MIU/m<sup>2</sup> each week to a maximum of 5 MIU/m<sup>2</sup>/day and ATRA 150 mg/m<sup>2</sup>/d x 7 days followed by 7 days rest. Treatment regimens will continue until the onset of accelerated or blast phase or relapse from CR or PR. Bone marrow aspiration and biopsy to monitor disease status are required at 3 and 6 months and every 6 months thereafter. Serial blood and urine specimens will be obtained for laboratory analysis.

**Progress:** No patients have been enrolled in this study at MAMC.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 93/166	<b>Status:</b> On-going
<b>Title:</b> SWOG 9303: Phase III Study of Radiation Therapy, Levamisole, and 5-Fluorouracil versus 5-Fluorouracil and Levamisole in Selected Patients With Completely Resected Colon Cancer		
<b>Start Date:</b> 09/03/93	<b>Est. Completion Date:</b> Oct 98	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Timothy P. Rearden, MC		
<b>Associate Investigators:</b>		
MAJ Kenneth A. Bertram, MC	LTC Luke M. Stapleton, MC	
MAJ Mark E. Robson, MC	MAJ Patrick L. Gomez, MC	
MAJ Richard C. Tenglin, MC	MAJ Robert B. Ellis, MC	
LTC Robert D. Vallion, MC	CPT James S. D. Hu, MC	
MAJ Richard F. Williams, MC	CPT Diana S. Willadsen, MC	
	CPT John R. Caton, MC	
<b>Key Words:</b> cancer:colon, irradiation, levamisole, 5-FU		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	12/17/93

**Study Objective:** To determine whether 5-FU, levamisole and radiation therapy results in superior overall survival when compared to 5-FU and levamisole without radiation therapy in the management of patients with completely resected pathologic stage T<sub>4</sub>BN<sub>0</sub>-2 colon cancer and selected patients with T<sub>3</sub>N<sub>1</sub>-2 colon cancer.

**Technical Approach:** This randomization clinical trial will compare radiation therapy, 5FU and levamisole with 5FU and levamisole in patients with completely resected colon cancer at high risk for local-regional recurrence and limited risk for system disease.

We will compare 5FU and levamisole, as delivered in the prior intergroup study, with one month of 5FU and levamisole followed by 5-5 1/2 weeks of 5FU, levamisole, and local-regional RT (45-50.4 Gy in 25-28 fractions), followed by 43 weeks of 5FU and levamisole.

**Progress:** One patient has been enrolled in this study at MAMC in FY95 and continues to be followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/111	<b>Status:</b> On-going
<b>Title:</b> SWOG 9304: Postoperative Evaluation of 5-FU by Bolus Injection vs 5-FU by Prolonged Venous Infusion Prior to and Following Combined Prolonged Venous + Pelvic XRT vs Bolus 5-FU +Leucovorin + ...		
<b>Start Date:</b> 05/06/94	<b>Est. Completion Date:</b> May 98	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Timothy P. Rearden, MC		
<b>Associate Investigators:</b>		
LTC Howard Davidson, MC	LTC Luke M. Stapleton, MC	
MAJ Patrick L. Gomez, MC	MAJ Kenneth A. Bertram, MC	
MAJ Robert B. Ellis, MC	MAJ Mark E. Robson, MC	
CPT James S. D. Hu, MC	MAJ Richard C. Tenglin, MC	
CPT Diana S. Willadsen, MC	LTC Robert D. Vallion, MC	
	MAJ Richard F. Williams, MC	
<b>Key Words:</b> Cancer:rectal, 5-FU, Leucovorin, Levamisole, radiotherapy		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> / /

**Study Objective:** 1) To compare the effectiveness of 5-FU by bolus injection vs. 5-FU by prolonged venous infusion given prior to and following combined pelvic x-ray (XRT) therapy + protracted venous infusion (PVI) vs. 5-FU by bolus injection plus LV plus LEV given prior to and following combined pelvic XRT plus bolus 5-FU plus LV in the treatment of modified Aster-Coller Stages B2, B3 and C rectal cancer. This will be evaluated in terms of survival and relapse-free survival.;2) To obtain descriptive information regarding relapse patterns and tolerance.

**Technical Approach:** Patients entering this study will be randomized to one of three treatment arms. Patients in all arms will receive pelvic radiotherapy. Those randomized to Arms A and B will receive concomitant 5-FU by PVI (225 mg/m<sup>2</sup>/d) during radiotherapy. Each patient will be randomly allocated to receive 5-FU +- LV and levamisole for 2 months prior to and for 2 months following combined chemo-radiotherapy. Patients will be randomized to chemotherapy prior to and following chemo-radiotherapy as follows: ;a. Arm A: bolus IV injection of 5-FU alone;b. Arm B: protracted venous infusion of 5-FU alone;c. Arm C: bolus 5-FU + LV + levamisole before and after pelvic radio therapy; bolus 5-FU + LV during pelvid radiotherapy. After completion of all therapy patients will be followed every 4 months X 2 years, then every 6 months X 4 years.

**Progress:** Three patients have been enrolled in this study at MAMC (2 in FY95). All three continue to be followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/162	<b>Status:</b> On-going
<b>Title:</b> SWOG 9307: Extended Administration of Oral Cyclophosphamide for the Treatment of Poor Prognosis Extensive Disease Small Cell Lung Cancer		
<b>Start Date:</b> 09/21/94	<b>Est. Completion Date:</b> Aug 93	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Robert D. Vallion, MC		
<b>Associate Investigators:</b>		
LTC Howard Davidson, MC	LTC Luke M. Stapleton, MC	
MAJ Timothy P. Rearden, MC	MAJ Kenneth A. Bertram, MC	
CPT James S. D. Hu, MC	MAJ Robert B. Ellis, MC	
MAJ Richard F. Williams, MC	CPT Diana S. Willadsen, MC	
	CPT John R. Caton, MC	
<b>Key Words:</b> Cancer:small cell lung, chemotherapy, etoposide, cyclophosphamide		
<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	//

**Study Objective:** (1) To estimate the response rate of extended oral administration of Etoposide and cyclophosphamide in poor prognosis extensive disease small cell lung cancer; (2) To evaluate the qualitative and quantitative toxicities of this regimen administered in a Phase II study; (3) To investigate possible correlations between peak and trough plasma etoposide levels versus complete response, toxicity, and survival.

**Technical Approach:** Untreated patients with extensive disease small cell lung cancer have a median survival of approximately 9 weeks. All patients will receive oral Etoposide and cyclophosphamide therapy once a day for 14 days. The dose for both chemotherapy agents will be 50 mg PO QD for the first cycle, with escalation allowed on later cycles. Ease of self administration and good subjective patient tolerance should make this combination of active agents particularly suitable for this patient population.

This treatment will continue for at least 6 months unless the patient experiences unacceptable side effects or if the disease becomes worse, at which time the physician will remove their from the study. Cranial Radiation will be given at the beginning of chemotherapy is cancer has already entered the brain.

**Progress:** Two patients were enrolled in this study at MAMC in FY95. Both patients died of the disease.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/106	<b>Status:</b> On-going
<b>Title:</b> SWOG 9308: Randomized Trial Comparing Cisplatin With Cisplatin Plus Intravenous Navelbine in the Treatment of Previously Untreated, Stage IV Non-small Cell Lung Cancer Patients		
<b>Start Date:</b> 05/06/94	<b>Est. Completion Date:</b> May 98	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Robert B. Ellis, MC		
<b>Associate Investigators:</b>		
LTC Howard Davidson, MC	LTC Luke M. Stapleton, MC	
MAJ Patrick L. Gomez, MC	MAJ Kenneth A. Bertram, MC	
MAJ Mark E. Robson, MC	MAJ Timothy P. Rearden, MC	
CPT James S. D. Hu, MC	MAJ Richard C. Tenglin, MC	
CPT Diana S. Willadsen, MC	LTC Robert D. Vallion, MC	
	MAJ Richard F. Williams, MC	
<b>Key Words:</b> Cancer:lung, non-small cell, cisplatin, Navelbine		
<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	//

**Study Objective:** 1) Compare the effect of cisplatin alone with that of intravenous Navelbine plus cisplatin on tumor response rate, survival, and time to treatment failure in patients with Stage IV non-small cell lung carcinoma. 2) Compare the toxicity of the two treatment regimens in patients with Stage IV non-small cell lung carcinoma.

**Technical Approach:** At the time of registration, patients will be stratified by LDH (normal vs abnormal) and classified by the following: a. disease status (measurable vs. evaluable), b. prior surgical resection or RT (yes vs. no), c. histology (squamous cell vs. large cell vs. adenocarcinoma vs. unspecified). They will then be randomized to either of two arms. Arm I patients will receive Cisplatin 100 mg/m<sup>2</sup> over 30 - 60 minutes every 28 days X 4. Arm II patients will receive Navelbine 25 mg/m<sup>2</sup> repeated weekly X 16 plus Cisplatin 100 mg/m<sup>2</sup> over 30 - 60 minutes every 28 days X 4. Patients will be evaluated every 3 months for the first year, every 6 months the second year, then yearly thereafter.

**Progress:** One patient has been enrolled in this study at MAMC in FY95 and continues to be followed. This study closed to patient accrual 1 June 95.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/170		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9313: Phase III Comparison of Adjuvant Chemotherapy With High-Dose Cyclophosphamide + Doxorubicin vs Sequential Doxorubicin Followed by Cyclophosphamide in High-Risk Breast.... 0-3 Positive Nodes					
<b>Start Date:</b> 09/21/94			<b>Est. Completion Date:</b> Sep 98		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Robert B. Ellis, MC					
<b>Associate Investigators:</b>					
LTC Howard Davidson, MC			LTC Luke M. Stapleton, MC		
MAJ Timothy P. Rearden, MC			MAJ Kenneth A. Bertram, MC		
LTC Robert D. Vallion, MC			CPT James S. D. Hu, MC		
MAJ Richard F. Williams, MC			CPT Diana S. Willadsen, MC		
			CPT John R. Caton, MC		
<b>Key Words:</b> cancer:breast, chemotherapy, cyclophosphamide, doxorubicin, positive nodes					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		/ /	

**Study Objective:** (1) To compare disease-free survival, overall survival, and toxicity of high-risk primary breast cancer patients with negative axillary lymph nodes or with one to three positive nodes treated with adjuvant high-dose chemotherapy with doxorubicin plus cyclophosphamide, versus high-dose sequential chemotherapy with doxorubicin followed by cyclophosphamide; (2) To obtain tumor tissue for biologic studies.

**Technical Approach:** Women with primary breast invasive adenocarcinoma, will be randomized to one of two treatments: 1) High dose doxorubicin + cyclophosphamide x 6 cycles, or 2) High dose sequential doxorubicin x 4 cycles, followed by high dose cyclophosphamide x 3. Women who are postmenopausal and have receptor + will receive Tamoxifen for 5 years.

**Progress:** No patients have been enrolled in this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/107	<b>Status:</b> On-going
<b>Title:</b> SWOG 9321: Standard Dose Versus Myeloablative Therapy for Previously Untreated Symptomatic Multiple Myeloma, Phse III		
<b>Start Date:</b> 05/06/94	<b>Est. Completion Date:</b> May 98	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT James S. D. Hu, MC		
<b>Associate Investigators:</b>		
LTC Howard Davidson, MC	LTC Luke M. Stapleton, MC	
MAJ Patrick L. Gomez, MC	MAJ Kenneth A. Bertram, MC	
MAJ Mark E. Robson, MC	MAJ Timothy P. Rearden, MC	
MAJ Richard C. Tenglin, MC	MAJ Robert B. Ellis, MC	
CPT Diana S. Willadsen, MC	LTC Robert D. Vallion, MC	
	MAJ Richard F. Williams, MC	
<b>Key Words:</b> Cancer:myeloma, BCNU, Cyclophosphamide, Cyclosporine, Dexamethasone, Doxorubicin, G-CSF, Interferon-alpha 2b, Melphalan, Mesna, Methotrexate, Prednisone, Vincristine		
<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	//

**Study Objective:** 1. To perform a randomized trial, in newly diagnosed patients with symptomatic multiple myeloma (MM), of standard therapy versus myeloablative therapy, in order to examine whether the greater tumor cytoreduction effected by intensive therapy and manifested by higher incidence of complete remission translates into extended overall survival and progression-free survival.;2. To randomize responding patients with  $\geq 75\%$  tumor cytoreduction to interferon-alpha 2b (IFN) versus no maintenance in order to evaluate the role of IFN in MM.

**Technical Approach:** Symptomatic patients of all stages of multiple myeloma with reasonable performance status will be randomized to high dose chemotherapy with autologous bone marrow transplant or standard VBMCP combination chemotherapy after induction VAD therapy. A required peripheral stem cell harvest will be done for those randomized to the ABMT arm for future high dose therapy if failure occurs. This will be an option for those randomized to the standard arm. Those patients that have an HLA compatible sibling donor will be eligible for allogeneic BMT. A second randomization will be done for those with continued greater than 75 percent regression of disease in the ABMT or standard chemotherapy arm while those receiving allo-BMT will be continued on GVHD prophylaxis.

**Progress:** No patients have been enrolled in this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/114	<b>Status:</b> On-going
<b>Title:</b> SWOG 9323: Laboratory/Clinical Correlative Studies in Non-Small Cell Lung Cancer: Ancillary Study to SWOG 9252 (INT-0115, E3590, RTOG 91-05, NCCTG 91-24-51)		
<b>Start Date:</b> 06/03/94	<b>Est. Completion Date:</b> May 98	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Timothy P. Rearden, MC		
<b>Associate Investigators:</b>		
LTC Howard Davidson, MC	LTC Luke M. Stapleton, MC	
MAJ Patrick L. Gomez, MC	MAJ Kenneth A. Bertram, MC	
MAJ Robert B. Ellis, MC	MAJ Mark E. Robson, MC	
CPT James S. D. Hu, MC	MAJ Richard C. Tenglin, MC	
CPT Diana S. Willadsen, MC	LTC Robert D. Vallion, MC	
	MAJ Richard F. Williams, MC	
<b>Key Words:</b> Cancer:lung, K-ras, p53, antigen, EHF receptor levels, p105, Factor 8		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> / /

**Study Objective:** 1) To determine the incidence of K-ras and p53 mutations; assess Group A blood antigen and EHF receptor levels; and assess p105 and Factor 8 levels in patients with completely resected Stage II or IIIa SCLC. 2) Correlate these results with patient histology, TNM stage, time to relapse, and survival.

**Technical Approach:** SWOG 9323 requires that tissue samples of lung cancer resected from each patient enrolled on SWOG 9252 be sent to three central research laboratories. Investigators will study the tissue samples for the tumor markers, K-ras, p-53, and others. Investigators are evaluating these tumor markers to determine if they can predict how patients might respond to treatment for non-small cell lung cancer.

**Progress:** No patients have been enrolled in this study at MAMC.

## Detail Summary Sheet

**Date:** 30 Sep 95      **Protocol No.:** 95/063      **Status:** Completed

**Title:** SWOG 9325: An Evaluation of the In Vivo Mechanism of Interferon Alfa-2b in the Context of ECOG Trial E1690 (SWOG 9111) Comparing Interferon Administered for 1 Year at high Dosage to Interferon Long...

**Start Date:** 01/20/95

**Est. Completion Date:** Nov 98

**Department:** SWOG

**Facility:** MAMC

**Principal Investigator:** CPT James S. D. Hu, MC

**Associate Investigators:**

LTC Howard Davidson, MC  
MAJ Timothy P. Rearden, MC  
LTC Robert D. Vallion, MC  
MAJ Richard F. Williams, MC

LTC Luke M. Stapleton, MC  
MAJ Kenneth A. Bertram, MC  
MAJ Robert B. Ellis, MC  
CPT Diana S. Willadsen, MC  
CPT John R. Caton, MC

**Key Words:** Cancer:melanoma, interferon

Accumulative	Est. Accumulative	Periodic Review:
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	/ /

**Study Objective :** 1) Study the In vitro and in vivo immunomodulatory effects of IFN alfa-2b on the cell function and phenotype of peripheral blood lymphocytes, and its in vitro effects on lymph node lymphocytes and autologous tumor cells; 2) Correlate treatment-induced changes in host immunomodulatory activity, tumor cell susceptibility and antigen expression with objective clinical response as measured by disease-free interval and patient survival; 3) Use the results of A and B above to support plausible mechanisms by which IFN alfa-2b may impact clinical response.

**Technical Approach :** The adjuvant treatment of metastatic melanoma to lymph nodes is being evaluated presently. SWOG protocol 9111 is randomizing patients to adjuvant therapy using high dose alpha interferon versus low dose interferon versus observation. It is hoped that this group of patients may benefit in terms of disease free and overall survival using this biologic therapy. Although there is clinical and laboratory evidence that alpha interferon promotes its effect on melanoma cells by immunomodulation, the exact in vitro and in vivo mechanisms are still not clear. SWOG study 9325 will attempt to identify these biologic mechanisms by analysis of resected tumor involved nodes and peripheral blood prior to, during and after alpha interferon in those patients that are randomized to those arms in SWOG 9111. Similarly the specimens for those patients on the observation arms will be sent.

**Progress :** This study closed to patient accrual 1 June 95. No patients were enrolled in this study at MAMC.



### Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 94/058

**Status:** On-going

**Title:** SWOG 9331 (E2192): Outcome Prediction by Histologic Grading in EST 1180 (SWOG 8294), Ancillary

**Start Date:** 02/04/94

**Est. Completion Date:** Nov 03

**Department:** SWOG

**Facility:** MAMC

**Principal Investigator:** MAJ Timothy P. Rearden, MC

**Associate Investigators:**

LTC Howard Davidson, MC

MAJ Patrick L. Gomez, MC

MAJ Robert B. Ellis, MC

CPT James S. D. Hu, MC

CPT Diana S. Willadsen, MC

LTC Luke M. Stapleton, MC

MAJ Kenneth A. Bertram, MC

MAJ Mark E. Robson, MC

MAJ Richard C. Tenglin, MC

LTC Robert D. Vallion, MC

MAJ Richard F. Williams, MC

**Key Words:** cancer:breast, histologic grading

**Accumulative**

**MEDCASE Cost:** \$0.00

**Est. Accumulative**

**OMA Cost:** \$0.00

**Periodic Review:**

//

**Study Objective:** 1) To evaluate the reproducibility of a combined histopathologic grading system of breast cancer. 2) To evaluate the ability of the grading system to predict time to treatment relapse (TTR) and survival. 3) To use multivariate analyses to evaluate the prognostic importance of the grading data relative to the other clinical and biological factors determined as part of SWOG 8294.

**Technical Approach:** This is a pathology study utilizing the patient set from SWOG 8294. Patients reviewed as part of that study (where cases with adequate specimens for flow cytometry were evaluated and provisionally graded) will be registered to this study. Slides will be reviewed by three investigators and cases will be grouped into 3 prognostic categories. The power calculation for testing the association of this grading system with survival will be based on the "2 degree of freedom" logrank test. The Cox proportional hazards model will also be used in the analysis to adjust the comparisons for effects of other factors.

**Progress:** Seven patients were enrolled in this study in FY94 and all are still being followed. This study closed to patient accrual 5 Oct 95.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/120	<b>Status:</b> Completed
<b>Title:</b> SWOG 9332: Phase III Trial of Adriamycin Versus Taxol Versus Taxol Plus Adriamycin Plus G-CSF in Metastatic Breast Cancer, Intergroup		
<b>Start Date:</b> 06/03/94	<b>Est. Completion Date:</b> May 98	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Robert B. Ellis, MC		
<b>Associate Investigators:</b>		
LTC Howard Davidson, MC	LTC Luke M. Stapleton, MC	
MAJ Patrick L. Gomez, MC	MAJ Kenneth A. Bertram, MC	
MAJ Mark E. Robson, MC	MAJ Timothy P. Rearden, MC	
CPT James S. D. Hu, MC	MAJ Richard C. Tenglin, MC	
CPT Diana S. Willadsen, MC	LTC Robert D. Vallion, MC	
	MAJ Richard F. Williams, MC	
<b>Key Words:</b> Cancer:breast, adriamycin, Taxol, G-CSF		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> / /

**Study Objective:** 1) To compare the objective response rate and time to progression of single-agent Adriamycin, single-agent Taxol, and the combination of Adriamycin and Taxol in patients with previously untreated metastatic breast cancer.;2) To compare the toxicity of Adriamycin, Taxol, and Adriamycin and Taxol given in combination.;3) To determine whether Taxol and Adriamycin exhibit crossover resistance to each other.;4) To compare the quality of life of patients who have received Taxol, Adriamycin, or the combination of Taxol and Adriamycin as first-line therapy for metastatic breast cancer.;5) To compare the quality of life of patients who have received Taxol or Adriamycin as second-line therapy.;6) To evaluate the relation of steady state Taxol levels to therapeutic response and toxicity.

**Technical Approach:** This is a randomized trial to compare the efficacy of single agent Taxol vs Adriamycin vs a Taxol and Adriamycin combination. Women with histologically confirmed breast carcinoma with progressive regional or metastatic cancer will be randomized between three Arms with single agent Adriamycin 60 mg/m<sup>2</sup> for 1 day, repeated every 21 days with crossover to Taxol with progression of disease; single agent Taxol 175 mg/m<sup>2</sup> every 3 weeks X 8 with crossover to single agent Adriamycin upon progression; or combination of Taxol 150 mg/m<sup>2</sup> and Adriamycin 50 mg/m<sup>2</sup> every 3 weeks X 8, plus G-CSF days 3 and 12. End points will be response, toxicity severity and quality of life characteristics.

**Progress:** This study closed to patient accrual 29 Sept 95. No patients were enrolled in this study at MAMC.

### Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 95/147

**Status:** On-going

**Title:** SWOG 9333: A Randomized Controlled Trial of Mitoxantrone & Etoposide vs Daunomycin & Cytosine Arabinoside as Induction Therapy in Patients Over Age 55 with Previously Untreated Acute Myeloid Leukemia

**Start Date:** 06/16/95

**Est. Completion Date:** Jun 99

**Department:** SWOG

**Facility:** MAMC

**Principal Investigator:** CPT James S. D. Hu, MC

**Associate Investigators:**

MAJ Kenneth A. Bertram, MC

LTC Robert D. Vallion, MC

CPT John R. Caton, MC

LTC Luke M. Stapleton, MC

MAJ Robert B. Ellis, MC

MAJ Richard F. Williams, MC

**Key Words:** Cancer:leukemia, myeloid, mitoxantrone, etoposide, daunomycin, cytosine arabinoside, over age 55

**Accumulative**

**MEDCASE Cost:** \$0.00

**Est. Accumulative**

**OMA Cost:** \$0.00

**Periodic Review:**

/ /

**Study Objectives:** To compare the complete remission (CR) rate, duration of survival and duration of relapse-free survival (time for CR until relapse or death) for patients aged 56 or older with acute myeloid leukemia (AML) treated with daunomycin (daunorubicin, DNR) and cytosine arabinoside (Ara-C) or with mitoxantrone (Mito) and etoposide. To assess the frequency and severity of toxicities and the durations of neutropenia, thrombocytopenia, and first hospitalization associated with the two induction chemotherapy regimens.

**Technical Approach:** Acute myelogenous leukemia in the elderly population is usually a fatal disease. Although complete remission rates are about 40-60% with standard chemotherapy induction, relapse rates are high and morbid and sometimes fatal toxicities will occur. This multi-center study aims to improve the remission rate and toxicity profile of induction chemotherapy for AML in the elderly using mitoxantrone and VP-16 and comparing it to standard daunorubicin and Ara-C followed by standard consolidation. Colony stimulating factors with GM-CSF will be given prophylactically as well as prophylactic antibiotics with Fluconazole, Ciprofloxacin, and Acyclovir. We expect 3-4 subjects per year and the entire multi-center recruitment is projected to be 100 per year.

**Progress :** No patients entered at MAMC

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/121		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9336: A Phase III Comparison Between Concurrent Chemotherapy Plus Radiotherapy, and Concurrent Chemotherapy Plus Radiotherapy Followed by Surgical Resection for Stage IIIA (N2) Non-Small Cell...					
<b>Start Date:</b> 06/03/94			<b>Est. Completion Date:</b> Jun 98		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Robert D. Vallion, MC					
<b>Associate Investigators:</b>			COL Daniel G. Cavanaugh, MC		
LTC Blaine R. Heric, MC			LTC Maceo Braxton Jr, MC		
MAJ Steven S. Wilson, MC			MAJ Rahul N. Dewan, MC		
LTC Luke M. Stapleton, MC			MAJ Nyun C. Han, MC		
MAJ Kenneth A. Bertram, MC			LTC Howard Davidson, MC		
			MAJ Patrick L. Gomez, MC		
<b>Key Words:</b> Cancer:non-small cell lung, chemotherapy, radiotherapy, surgical resection					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		/ /	

**Study Objective:** 1) Assess whether concurrent chemotherapy and radiotherapy followed by surgical resection results in a significant improvement in progression-free, median, and long-term (2 year, 5 year)s survival compared to the same chemotherapy plus standard radiotherapy alone for patients with stage IIIa (N2-positive) non-small cell lung cancer.;2) Evaluate the patterns of local and distant failure for patients enrolled in each arm of the study, in order to assess the impact of the therapy on local control and distant metastases.;3) To obtain exploratory descriptive information on the relationship of tobacco use, alcohol use and dietary patterns on toxicity and outcomes in males and females.

**Technical Approach:** Patients with biopsy-proven Stage IIIa Non-Small Cell carcinoma will be randomized to one of two arms. Arm I and II patients will receive Induction Radiotherapy (45 Gy + concurrent induction chemotherapy (CT) of Cisplatin 50 mg/m<sup>2</sup> IVPB days 1, 8, 29, 36 and VP-16 50 mg/m<sup>2</sup> IVPB, days 1-5, 29-33. Arm I patients will be re-evaluated 2-4 weeks after completion of induction and Arm II will be re-evaluated 7 days before completion of induction. All patients, after re-evaluation, will proceed to Registration 2. If there is no evidence of local progression or distant metastases patients will be assigned options 3 or 4 (Arm I) or option 5 (Arm II. Option 3 consists of surgery plus 2 additional cycles CT starting 4-6 weeks postoperatively, Option 4 of 2 additional cycles CT at least 3 weeks after cycle 2 and Option 5 of continuing RT with no break and beginning 2 additional cycles of CT 3 weeks after cycle 2, day 8. RT boost field will be planned by CT scan. The major endpoints will be median, 2-year and 5-year progression-free and overall survival. Evaluation of patterns of relapse is a secondary endpoint.

**Progress:** Two patients were enrolled in this study at MAMC in FY95. Both patients are now deceased.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/122	<b>Status:</b> Completed
<b>Title:</b> SWOG 9339: Evaluation of Topotecan in Esophageal Carcinoma, Phase II		
<b>Start Date:</b> 06/03/94	<b>Est. Completion Date:</b> May 98	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Timothy P. Rearden, MC		
<b>Associate Investigators:</b>		
LTC Howard Davidson, MC	LTC Luke M. Stapleton, MC	
MAJ Patrick L. Gomez, MC	MAJ Kenneth A. Bertram, MC	
MAJ Robert B. Ellis, MC	MAJ Mark E. Robson, MC	
CPT James S. D. Hu, MC	MAJ Richard C. Tenglin, MC	
CPT Diana S. Willadsen, MC	LTC Robert D. Vallion, MC	
	MAJ Richard F. Williams, MC	
<b>Key Words:</b> Cancer:esophageal, topotecan		
<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	/ /

**Study Objective:** To evaluate the response rate of esophageal carcinoma treated with topotecan; and to evaluate the qualitative and quantitative toxicities of topotecan administered in a Phase II study.

**Technical Approach:** Patients enrolled in this study will receive Topotecan 1.5 mg/m<sup>2</sup> via continuous infusion IV over 24 hours on days 1, 8, 15, and 22. The retreat interval will be every 42 days (weekly X 4 weeks; 2 week rest period). Patients will continue this treatment schedule as long as they show complete remission, partial remission, or stable disease. Response assessments are to be performed every cycle along with laboratory analysis.

**Progress:** No patients have been enrolled in this study at MAMC. This study closed to patient entry 1 Dec 94.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/091		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9340: A Phase III Randomized Study of Radiotherapy With or Without BUdR Plus Procarbazine, CCNU, and Vincristine (PCV) for the Treatment of Anaplastic Astrocytomas					
<b>Start Date:</b> 03/17/95			<b>Est. Completion Date:</b> Feb 99		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Diana S. Willadsen, MC					
<b>Associate Investigators:</b>					
LTC Howard Davidson, MC			LTC Luke M. Stapleton, MC		
MAJ Timothy P. Rearden, MC			MAJ Kenneth A. Bertram, MC		
CPT James S. D. Hu, MC			MAJ Robert B. Ellis, MC		
MAJ Richard F. Williams, MC			LTC Robert D. Vallion, MC		
			CPT John R. Caton, MC		
<b>Key Words:</b> Cancer:astrocytoma, radiotherapy, BUdR, Procarbazine, CCNU, Vincristine					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		//	

**Study Objective:** This study will determine if the experimental drug BUdR given before and during radiation therapy, followed by the chemotherapy drugs procarbazine, CCNU, and vincristine can slow the growth of your tumor. You have been asked to participate in this study because of the type and location of your brain tumor.

**Approach:** This study involves a random assignment to one of two treatment arms. All patients will receive RT and PCV chemotherapy and half will also receive BUdR. Treatment 1: If assigned to receive radiation therapy followed by chemotherapy, subject will be given radiation therapy to the brain five days a week for six to seven weeks. Within two weeks after completing radiation therapy, subject will receive CCNU by mouth for one day (day 1 of each cycle). One week later they will be given procarbazine by mouth every day for two weeks (days 8 through 21). On days 8 and 29, they will be given vincristine by vein. Subject will continue to receive CCNU, procarbazine, and vincristine every six to eight weeks on this schedule for a period of one year (or at least six but no more than eight times) unless the disease worsens or complications arise. Treatment 2: If assigned to receive the radiation therapy plus the drug BUdR, the subject will be given BUdR by vein continuously for four days just before starting the first week of radiation therapy and for four days per week starting on day 4 or 15 of radiation therapy each week during the first five weeks of therapy. BUdR will be given either in the hospital or on an outpatient basis. If hospitalization is required, BUdR will be delivered through a vein in the arm. If not hospitalized, BUdR will be delivered by a portable infusion pump through a vein in the neck and shoulder area. A central venous catheter may be recommended for drug delivery. Within two weeks after completing radiation and BUdR therapy, the subject will receive CCNU by mouth for one day (day 1). One week later, the subject will be given procarbazine by mouth every day for two weeks (days 8 through 21). On days 8 and 29, the subject will be given vincristine by vein and will continue to receive CCNU, procarbazine, and vincristine every six to eight weeks on this schedule for a period of one year (or for at least six but no more than eight times) unless your disease worsens or complications arise. Blood counts and regularly performed physical examinations and laboratory tests will be taken to measure progress and toxicity from these treatments.

**Progress :** No patients have been enrolled in this study at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/092		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9341: High Dose Ifosfamide (HDI) with Mesna and Granulocyte-Colony Stimulating Factor (rhG-CSF) in Unresectable Malignant Mesothelioma					
<b>Start Date:</b> 03/17/95			<b>Est. Completion Date:</b> Feb 99		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Diana S. Willadsen, MC					
<b>Associate Investigators:</b>					
LTC Howard Davidson, MC			LTC Luke M. Stapleton, MC		
MAJ Timothy P. Rearden, MC			MAJ Kenneth A. Bertram, MC		
CPT James S. D. Hu, MC			MAJ Robert B. Ellis, MC		
MAJ Richard F. Williams, MC			LTC Robert D. Vallion, MC		
			CPT John R. Caton, MC		
<b>Key Words:</b> Cancer:mesothelioma, ifosfamide, GCSF					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		/ /	

**Study Objective:** 1) to assess the activity of high-dose ifosfamide and measna with recombinant human G-CSF (rhG-CSF) in patients with unresectable malignant mesothelioma. 2) To evaluate the toxicity pattern of high-dose ifosfamide/mesna/rhG-CSF given according to this outpatient schedule.

**Approach:** Subjects will receive ifosfamide and mesna in a solution through the vein. Both drugs will be given daily for 5 days in a row. rhG-CSF will be given by subcutaneous injection, days 6-15. Treatments will be repeated every 21 days as long as disease does not get worse. If disease worsens, subject will be taken off study and offered another treatment. If disease stays the same or improves slightly, subject will continue to receive treatment at the highest tolerable dose for at least two more cycles (one cycle is equal to 21 days) or until disease worsens. If disease completely disappears, subject will receive an additional two cycles of therapy once the disappearance of the disease has been confirmed by laboratory tests necessary to follow disease. At that point, treatment will be stopped and the subject will be followed to see if disease reappears.

**Progress :** No patients have entered this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 94/123		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9348: Evaluation of the Standard DCNU/DTIC/Cisplatin/Tamoxifen Regiment in Disseminated Malignant Melanoma, Phase II					
<b>Start Date:</b> 06/03/94			<b>Est. Completion Date:</b> Jun 98		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT James S. D. Hu, MC					
<b>Associate Investigators:</b>			LTC Luke M. Stapleton, MC		
LTC Howard Davidson, MC			MAJ Kenneth A. Bertram, MC		
MAJ Patrick L. Gomez, MC			MAJ Timothy P. Rearden, MC		
MAJ Mark E. Robson, MC			MAJ Robert B. Ellis, MC		
MAJ Richard C. Tenglin, MC			LTC Robert D. Vallion, MC		
CPT Diana S. Willadsen, MC			MAJ Richard F. Williams, MC		
<b>Key Words:</b> Cancer:melanoma, BCNU, DTIC, Cisplatin, Tamoxifen					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	/ /	

**Study Objective:** To estimate the response rate of the combination of BCNU/DTIC/cisplatin/tamoxifen in patients with disseminated malignant melanoma in order to select the appropriate regimen for combination with alpha-interferon in a future Phase III trial; and to accurately determine the toxicities of this drug combination in order to assess its feasibility in a future Phase III trial.

**Technical Approach:** Participants in this study must not be receiving or planning to receive concomitant biologic therapy, surgery, radiation therapy, hormonal therapy, or other chemotherapy or other treatment while on this protocol. DTIC, 220 mg/m<sup>2</sup> IV on days 1-3 & 22-24; cisplatin, 25 mg/m<sup>2</sup> IV on days 1-3 & 22-24; BCNU, 150 mg/m<sup>2</sup> IV on day 1; and tamoxifen, 110 mg/m<sup>2</sup> B.I.D. daily will be given throughout treatment. Retreatment interval is 6 weeks. Patients will continue on this regimen until they fulfill one of the defined criteria for removal from treatment. Patients will undergo frequent laboratory evaluations for toxicities. After completion of therapy, patients will be followed every three months for one year, every six months for the next two years, and annually thereafter.

**Progress:** Two patients have been enrolled in this study at MAMC in FY95 and continue to be followed. This study closed to patient accrual 1 Apr 95.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/024		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9349: A Randomized Phase II Trial of CHOP with G-CSF Support or ProMACE-CytaBOM With G-CSF Support for Treatment of Non-Hodgkin's Lymphoma					
<b>Start Date:</b> 11/18/94			<b>Est. Completion Date:</b> Nov 98		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT James S. D. Hu, MC					
<b>Associate Investigators:</b>					
LTC Howard Davidson, MC			LTC Luke M. Stapleton, MC		
MAJ Timothy P. Rearden, MC			MAJ Kenneth A. Bertram, MC		
LTC Robert D. Vallion, MC			MAJ Robert B. Ellis, MC		
MAJ Richard F. Williams, MC			CPT Diana S. Willadsen, MC		
			CPT John R. Caton, MC		
<b>Key Words:</b> Cancer:Non-Hodgkin's lymphoma, CHOP, ProMACE-CytaBOM, G-CSF					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		/ /	

**Study Objectives:** To evaluate the effectiveness of the dose intense CHOP chemotherapy regimen with G-CSF support and the dose intense ProMACE-CytaBOM chemotherapy regimen with G-CSF support in previously untreated patients with intermediate and high grade non-Hodgkin's lymphomas. The effectiveness of the regimens will be based on the estimate of the complete response rate, the time to treatment failure, and ultimately overall survival. To assess the toxicities and side effects associated with the regimens. Also to further utilize the central serum and tissue repositories enabling clinicopathologic correlations with the results of studies on the material collected.

**Technical Approach:** This study attempts to assess whether dose intense CHOP or Promace-CytaBOM with growth factor support will have any effect on improvement of standard first line therapy in non-Hodgkins lymphoma. Ninety-eight patients will be accrued for each of the two arms. This number of patients will allow for both the complete response rate and probability of treatment failure two years after treatment to be estimated to within at most +/- .10 for each measure. A successful outcome for either regimen is one that has a true probability of 60% or higher of patients being alive without disease at two years. No formal statistical comparisons between arms will be made.

**Progress :** No patients have been enrolled in this study at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/003	<b>Status:</b> On-going
<b>Title:</b> SWOG 9401: A Controlled Phase III Evaluation of 5-FU Combined with Levamisole and Leucovorin as Surgical Adjuvant Treatment Following Total Gross Resection of Metastatic Colorectal Cancer		
<b>Start Date:</b> 10/21/94	<b>Est. Completion Date:</b> Oct 98	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Timothy P. Rearden, MC		
<b>Associate Investigators:</b>		
LTC Howard Davidson, MC	LTC Luke M. Stapleton, MC	
MAJ Robert B. Ellis, MC	MAJ Kenneth A. Bertram, MC	
LTC Robert D. Vallion, MC	CPT James S. D. Hu, MC	
MAJ Richard F. Williams, MC	CPT Diana S. Willadsen, MC	
	CPT John R. Caton, MC	
<b>Key Words:</b> cancer:breast, chemotherapy, doxorubicin, Taxol, positive nodes		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> / /

**Study Objective:** To determine in patients who have undergone complete gross surgical resection of metastatic colorectal cancer whether postoperative adjuvant chemotherapy with a new regimen of 5-fluorouracil (5-FU) plus leucovorin plus levamisole will result in improved survival compared to postoperative adjuvant chemotherapy with a standard 5-FU plus levamisole regimen.

**Technical Approach:** Patients will be randomly selected to treatment Arm I or treatment Arm II. Arm I consists of the standard regimen of 5-FU given by rapid intravenous infusion for 5 consecutive days, plus levamisole given by mouth three times daily for three consecutive days every other week for one year. Arm II is a new chemotherapy regimen which adds leucovorin in addition to the 5-FU and levamisole. 5-FU and leucovorin are given by rapid intravenous injection for five consecutive days every four to five weeks for one year. Levamisole is given by mouth three times per day for three days in a row every two weeks during the first two months, then every 2-3 weeks for a total of one year.

**Progress :** No patients have been enrolled in this study at MAMC.

## Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 95/093

**Status:** On-going

**Title:** SWOG 9402: Phase III Intergroup Randomized Comparison of Radiation Alone vs Pre-Radiation Chemotherapy for Pure and Mixed Anaplastic Oligodendrogliomas

**Start Date:** 03/17/95

**Est. Completion Date:** Feb 99

**Department:** SWOG

**Facility:** MAMC

**Principal Investigator:** CPT Diana S. Willadsen, MC

**Associate Investigators:**

LTC Howard Davidson, MC  
MAJ Timothy P. Rearden, MC  
CPT James S. D. Hu, MC  
MAJ Richard F. Williams, MC

LTC Luke M. Stapleton, MC  
MAJ Kenneth A. Bertram, MC  
MAJ Robert B. Ellis, MC  
LTC Robert D. Vallion, MC  
CPT John R. Caton, MC

**Key Words:** Cancer:oligodendroglioma, radiotherapy, CCNU, vincristine, procarbazine, vincristine

**Accumulative**

**MEDCASE Cost:** \$0.00

**Est. Accumulative**

**OMA Cost:** \$0.00

**Periodic Review:**

//

**Study Objective:** 1) overall survival 2) compare time to tumor progression between the two arms 3) the frequency of severe ( $\geq$  grade 3) toxicities will be examined. 4) compare quality of life and neurologic function between the two arms. 5) identify the key histopathologic criteria necessary to make the diagnosis of anaplastic oligodendroglioma and mix oligo-astrocytoma; evaluate the diagnostic and prognostic relevance of chromosomal alterations; evaluate the diagnostic and prognostic relevance of DNA ploidy and indices of proliferation including percent S and percent G2M; study the diagnostic and prognostic relevance of immunohistochemical markers of cellular function and/or glial development; and evaluate the transnational relevance of tumor suppressor genes and oncogenes.

**Technical Approach:** This is a non-blinded randomized intergroup study and is different from other randomized trials for malignant glioma in three respects. First, it will evaluate the role of adjuvant chemotherapy in a recognizable subset of patients with malignant glioma, those with oligodendroglial differentiation. Second, the RT treatment volume will be based on a postoperative pre-randomization MR image, rather than the customary preoperative diagnostic CT or MR. Third, in the experimental arm of this study, chemotherapy will be given prior to RT. This departure from standard management can be justified based on the high rate of response of pure and mixed oligodendrogliomas to PCV, and successful piloting of this approach at several centers. There are potential advantages to pre-RT PCV: chemotherapy may be more effective when given prior to radiation; effective chemotherapy may result in substantial reductions in tumor size prior to RT; and RT may control small tumors more effectively than larger ones. Patients whose tumors progress on chemotherapy will proceed to RT immediately. Several other important features of this study are central pathology review prior to randomization, central radiology review to assess response to PCV and to substantiate tumor progression, and a quality of life assessment (QLA) to document the acute and chronic toxicities of chemotherapy and radiation including effects on cognitive function. Surgery and radiotherapy plus or minus PCV may adversely affect a patient's physical and emotional functioning. The Karnofsky performance status (KPS) will measure physical well-being. To complement KPS, the Mini-Mental Status exam (MMSE) will be administered to patients to assess

cognitive ability. These tools will permit us to assess the effect of therapy and disease on these domains in both the acute and long-term settings. Assessment of differences in quantitative survival between the two therapeutic regimens supplemented with qualitative survival by the assessment of KPS, MMSE, and QLA.

Progress : No patients have been enrolled in this study at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 94/163	<b>Status:</b> On-going
<b>Title:</b> SWOG 9410 (INT 0148): Doxorubicin Dose Escalation, With or Without Taxol, As Part of the CA Adjuvant Chemotherapy Regimen for Node Positive Breast Cancer: A Phase III Intergroup Study		
<b>Start Date:</b> 09/21/94	<b>Est. Completion Date:</b> Sep 98	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Robert B. Ellis, MC		
<b>Associate Investigators:</b>		
LTC Howard Davidson, MC	LTC Luke M. Stapleton, MC	
MAJ Timothy P. Rearden, MC	MAJ Kenneth A. Bertram, MC	
LTC Robert D. Vallion, MC	CPT James S. D. Hu, MC	
MAJ Richard F. Williams, MC	CPT Diana S. Willadsen, MC	
	CPT John R. Caton, MC	
<b>Key Words:</b> cancer:breast, chemotherapy, doxorubicin, Taxol, positive nodes		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> / /

**Study Objective:** To determine (1) whether dose escalation of doxorubicin used as an adjuvant with cyclophosphamide in patients with early breast cancer will increase disease free and overall survival; (2) whether the use of Taxol as a single agent after the completion of 4 cycles of cyclophosphamide and doxorubicin in combination will further improve disease-free and overall survival compared to cyclophosphamide and doxorubicin alone; (3) if Taxol following standard dose cyclophosphamide and doxorubicin will be as effective or more effective than high dose cyclophosphamide and doxorubicin without Taxol; (4) to access the toxicity of the different doses of cyclophosphamide and doxorubicin with and without Taxol using the end point of life threatening or lethal toxicity; (5) whether the longer duration of chemotherapy treatment for patients randomized to receive Taxol is associated with a reduction in local recurrence in patients with lumpectomy and radiotherapy.

**Technical Approach:** Women with breast cancer, who have been treated with either mastectomy or segmentectomy will receive adjuvant chemotherapy. All patients will receive 4 courses of cyclophosphamide and doxorubicin (21 day cycle), but the doxorubicin dose will vary depending upon the randomization. Patients randomized to high dose doxorubicin will also receive G-CSF & ciprofloxacin. Some women will be randomized to receive Taxol after 4 cycles of AC chemotherapy is completed. They will receive taxol day 1 of a 21 day cycle for 4 cycles. Women with ER positive tumors will be given tamoxifen for 5 years.

**Progress:** Six patients have been enrolled in this study at MAMC in FY95. All six continue to be followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95		<b>Protocol No.:</b> 95/094		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9415: Phase III Randomized Trial of 5-FU/Leucovorin/Levamisole versus 5-FU Continuous Infusion Levamisole as Adjuvant Therapy for High-Risk Resectable Colon Cancer, Intergroup					
<b>Start Date:</b> 03/17/95			<b>Est. Completion Date:</b> Feb 99		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Timothy P. Rearden, MC					
<b>Associate Investigators:</b>			LTC Luke M. Stapleton, MC		
LTC Howard Davidson, MC			MAJ Kenneth A. Bertram, MC		
MAJ Robert B. Ellis, MC			CPT James S. D. Hu, MC		
LTC Robert D. Vallion, MC			CPT Diana S. Willadsen, MC		
MAJ Richard F. Williams, MC			CPT John R. Caton, MC		
<b>Key Words:</b> Cancer:colon, 5-FU, leucovorin, levamisole					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		/ /	

**Study Objective:** To compare the effectiveness of bolus 5-FU, leucovorin, levamisole versus continuous infusion 5-FU, levamisole as adjuvant therapy for patients with Stage B2, C1 or C2 colon cancer. This will be measured in terms of overall survival. Disease-free survival will be a secondary endpoint.

**Approach:** This trial is an intergroup trial involving the Southwest Oncology Group, Eastern Cooperative Oncology Group and the Cancer and Leukemia Group B. Based on previous experience with accrual to INT-0089, and assuming that roughly 1/3 of patients eligible for that study will be entered we anticipate an annual accrual of approximately 600 patients having curative resection of B2, C1, or C2 colon cancer. The primary objective of this study is to compare the survival in patients with high risk resectable colon surgery treated in an adjuvant setting with either 5-FU, leucovorin, levamisole or continuous infusion 5-FU, levamisole. The continuous infusion arm would be judged superior if the true increase in survival is 35%. A secondary endpoint will be disease-free survival. The dose of continuous infusion 5-FU selected for this study of 250 mg/m<sup>2</sup>/d is currently being piloted at an individual institution, and is lower than the common dose of 300 mg/m<sup>2</sup>/d, which required dose reductions in a previous pilot. In order to verify the appropriateness of this dose in the intergroup setting, we will evaluate toxicity and compliance in the first 40 patients randomized to the continuous infusion arm. Should the frequency of dose reductions or toxicities warrant concern, the study may be amended or temporarily closed while the continuous infusion therapy is reassessed.

**Progress :** No patients have been enrolled in this study at MAMC.

## Detail Summary Sheet

**Date:** 30 Sep 95

**Protocol No.:** 95/151

**Status:** On-going

**Title:** SWOG 9416: A Phase II Intergroup Trial of Induction Chemoradiotherapy Followed by Surgical Resection for Non-Small Cell Lung Cancer Involving the Superior Sulcus (Pancoast Tumors)

**Start Date:** 06/16/95

**Est. Completion Date:** Jun 99

**Department:** SWOG

**Facility:** MAMC

**Principal Investigator:** LTC Robert D. Vallion, MC

**Associate Investigators:**

MAJ Kenneth A. Bertram, MC

CPT James S. D. Hu, MC

CPT John R. Caton, MC

LTC Luke M. Stapleton, MC

MAJ Robert B. Ellis, MC

MAJ Richard F. Williams, MC

**Key Words:** Cancer:non-small cell lung, radiation, cisplatin, VP-16

**Accumulative**

**MEDCASE Cost:** \$0.00

**Est. Accumulative**

**OMA Cost:** \$0.00

**Periodic Review:**

//

**Study Objectives:** To assess the feasibility and toxicity of treating patients who have pancoast tumors without mediastinal or supraclavicular nodal involvement (T3-4, N0-1) with Cisplatin and VP-16 for two cycle, concurrent with a program of continuous, fractionated chest radiation followed by surgical resection and boost chemotherapy. To assess the objective response rate, resectability rate, and proportion of patients free of microscopic residual disease after such an approach.

**Technical Approach:** This oncology group protocol is a Phase II chemoradiation induction of superior sulcus (pancoast) tumors, non-small cell lung cancer followed by surgical resection. There are no extraordinary requirements of this study. This study should recruit 4-5 MAMC patients a year, 18 or older, and of either sex with selected Stage IIIa (T3, N0-1) or Stage IIIb (T4, N0-1) tumors involving the superior sulcus. The main goals of this study are to estimate the response, toxicity, and resectability rates following the combined chemoradiotherapy. We plan to accrue a total of 99 patients which will allow for estimation of rates and provide a sufficient number which will undergo resection. The precision of estimation of rates within stage IIIA or IIIB will depend on the breakdown by stage.

**Progress :** No patients have been enrolled in this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/152	<b>Status:</b> On-going
<b>Title:</b> SWOG 9424: A Phase II Trial of High Dose Tamoxifen Plus Cisplatin Chemotherapy in Metastatic Non-small Cell Lung Cancer		
<b>Start Date:</b> 06/15/95	<b>Est. Completion Date:</b> Jun 99	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Robert D. Vallion, MC		
<b>Associate Investigators:</b>		
MAJ Kenneth A. Bertram, MC	LTC Luke M. Stapleton, MC	
CPT James S. D. Hu, MC	MAJ Robert B. Ellis, MC	
CPT John R. Caton, MC	MAJ Richard F. Williams, MC	
<b>Key Words:</b> Cancer:Non-small cell lung, Tamoxifen, Cisplatin		
<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	//

**Study Objective :** 1) To evaluate the efficacy of the protein kinase modulator high-dose tamoxifen in combination with cisplatin in the treatment of men and women with metastatic non-small cell lung cancer (NSCLC). 2) To assess the toxicity of the combination. 3) To estimate the response rate with each gender and to characterize baseline tumor properties such as estrogen/progesterone receptor status, kinase c expression, and mdm-1 glycoprotein expression.

**Technical Approach :** Patients will receive tamoxifen in tablet form for 28 days, twice a day for seven days. Cisplatin will be given intravenously with two pints of fluid before and after cisplatin. Cisplatin is administered over a period of an hour on days 4 and 11. Routine laboratory test will be done including blood tests, x-rays and scans. After reaching two cycles of treatments, patients will be tested for a response. If a complete response is found, patient will receive an additional two cycles of treatment and then therapy will stop. If after two cycles there is a partial response, patient will receive up to 6 more cycles of treatment. If the disease remains stable of the two cycles, two more cycles will be given. If the disease has not improved, patient will be taken of study.

**Progress :** No patients have been enrolled in this study at MAMC.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/026	<b>Status:</b> Completed
<b>Title:</b> SWOG 9429: Phase II Trial of Carboplatin and VP-16 With Concurrent Radiation for Poor-Risk Stage III Non-small Cell Lung Carcinoma		
<b>Start Date:</b> 11/18/94	<b>Est. Completion Date:</b> Aug 93	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Robert D. Vallion, MC		
<b>Associate Investigators:</b>		
LTC Howard Davidson, MC	LTC Luke M. Stapleton, MC	
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	CPT John R. Caton, MC	
<b>Key Words:</b> Cancer:small cell lung, radiation, chemotherapy, carboplatin, VP-16		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> / /

**Study Objectives:** To assess the median and two-year survival and progression-free survival of poor-risk patients with Stage III Non-small cell lung carcinoma treated with concurrent radiation, carboplatin and VP-16. To assess the response rate and pattern of local and distant failure. To assess the toxicity of this regimen in this group of poor-risk patients.

**Technical Approach:** This is a phase two trial of carboplatin and VP-16 with concurrent radiation for poor-risk Stage IIIA/IIIB patients with non-small cell lung cancer. The primary goal of this study is to estimate the two-year survival in these poor-risk patients. Patients will receive four cycles of chemotherapy at 4 week intervals with radiation therapy to 60 cGy to the tumor and involved areas. Usual toxicity and re-evaluation schedules will be used. We plan to accrue 50 eligible patients, which will allow for estimation of the survival rate (given complete follow-up) to within 14% with a 95% confidence interval. Fifty patients will also be sufficient to estimate response and toxicity rates to within 14%. Any adverse event occurring with at least a 5% probability is likely to be seen at least once (92% chance).

**Progress:** This study closed to patient accrual 1 Sept 95. No patients were enrolled at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 95/148	<b>Status:</b> On-going
<b>Title:</b> SWOG 9501: A Phase II Trial of Fludarabine and Mitoxantrone (FN) for Treatment of Non-Hodgkin's Lymphoma		
<b>Start Date:</b> 06/16/95	<b>Est. Completion Date:</b> Jun 99	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT James S. D. Hu, MC		
<b>Associate Investigators:</b>		
MAJ Kenneth A. Bertram, MC	LTC Luke M. Stapleton, MC	
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CPT John R. Caton, MC	MAJ Richard F. Williams, MC	
<b>Key Words:</b> Cancer:Non-Hodgkin's lymphoma, fludarabine, mitoxantrone		
<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	//

**Study Objectives:** To estimate the two-year progression-free survival rate in patients with previously untreated low-grade non-Hodgkin's lymphoma treated with fludarabine and mitoxantrone. To evaluate the toxicity of fludarabine and mitoxantrone in this group of patients.

**Technical Approach:** Advanced low grade lymphoma is an incurable disease. Although high responses are reported, long term, disease-free survival is not common and patients will eventually relapse. Many different chemotherapy modalities have been used and although overall response rates are different, the overall survival is not significantly changed. High dose therapy has been used and is undergoing active investigation. Newer agents have been introduced to attempt to improve the disease free and overall survival of patients with low grade lymphomas. This study attempts to use Fludarabine and Mitoxantrone in combination in newly diagnosed, advanced, low-grade lymphoma patients to see if any efficacy can be achieved in a single arm phase II study. All patients will receive prophylaxis with Septra for pneumocystis. All patients registered for this protocol will be eligible for serum and tissue submission on SWOG protocols 8947 and 8819 respectively.

**Progress :** No patients have been enrolled in this study at MAMC.

**DETAIL SHEETS FOR PROTOCOLS**

**UNIVERSITY OF WASHINGTON NEURO-ONCOLOGY  
GROUP**

## Detail Summary Sheet

<b>Date:</b> 30 Sep 95	<b>Protocol No.:</b> 89/013	<b>Status:</b> On-going
<b>Title:</b> UWNG 88-01: Phase II Study of High Dose Methotrexate and Craniospinal Irradiation for the Treatment of Primary Lymphoma of the Central Nervous System		
<b>Start Date:</b> 01/20/89	<b>Est. Completion Date:</b> Nov 92	
<b>Department:</b> UWNG/	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Howard Davidson, MC		
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<b>Key Words:</b> lymphoma:central nervous system,chemoradiotherapy,methotrexate		
<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$328.00	12/17/93

**Study Objective:** To evaluate this regimen, the end-points of analysis will be: time to progression of disease from beginning of therapy, response rates and disease stabilization rates, survival time measured from the beginning of therapy, quality of life, and activity level measured by Karnofsky performance status.

**Technical Approach:** Patients must have a non-Hodgkin's lymphoma of the central nervous system with adequate renal, bone marrow, and liver function, and a performance status of >70%. HIV antibody titer must be negative. No prior chemotherapy or radiotherapy is permitted.

Methotrexate, 4 g/m<sup>2</sup>, will be administered over a four hour period. Calcium leucovorin, 25 mg, will be administered beginning 20 hours after completion of the methotrexate infusion and repeated for 8 doses, parenterally, on an every 6 hour basis, following which an additional four doses will be administered every six hours by mouth. The methotrexate regimen will be administered every two weeks for three courses. Radiotherapy will begin two weeks after completion of methotrexate and will consist of 5040 cGy to whole brain at 180 cGy/fraction (28 fractions) and 3060 cGy at 170 cGy/fraction (19 fractions) to spinal axis. Time to progression will be measured from the initiation of therapy until progression is documented. At that time, the patient will be removed from the protocol and can be treated with other therapy as indicated. Patients will be followed until death.

**Progress:** The protocol has been closed to patient entry. One patient was enrolled and is still being followed.

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